CALCIFICATION OF THE CORPUS STRIATUM AND DENTATE NUCLEI OCCURRING IN A FAMILY

BY

J. FOLEY

From the Neurological Department, St. George's Hospital, London

Dense symmetrical calcification of the corpus striatum is rare, but of some general interest for two reasons. First, in a significant number of the reported cases this apparently degenerative condition is closely linked with a metabolic disorder, hypoparathyroidism, which may be idiopathic, parathyroprivic, or of the variety in which the parathyroid glands are histologically normal but the body is unable to respond to parathormone (Albright's pseudohypoparathyroidism). Secondly, in no other degenerative disease limited to a neurophysiological system can the process be visualized radiologically. In contrast with the rare gross calcification under discussion, microscopically demonstrable calcification occurring on a basis of hyaline degeneration in and around the vessels in these regions is very common, and can, indeed, be found to a certain extent in normal brains. Such calcification formerly attracted much attention in certain inflammatory conditions, chorea, encephalitis lethargica, polio-encephalitis, and cerebral malaria; in intoxications with carbon monoxide, nitrous oxide, and lead; in degenerative conditions such as amaurotic idiocy and the progressive pigmentary pallidonigral degeneration of Hallervorden and Spatz; and in certain metabolic and endocrine disorders (other than hypoparathyroidism) such as Addison's disease, cretinism, myxoedema, and severe pernicious anaemia. Calcification in the basal ganglia gross enough to be visible radiologically occurs in two main groups of conditions: in association with parathyroid insufficiency, as is now well known, and in certain rare familial instances. It is in the latter, of which the family reported below is the third in the literature, that the calcification attains its most florid form.

Case Report

Mrs. M.E., aged 60, was admitted to the Maida Vale Hospital for Nervous Diseases, London, under the care of Dr. P. H. Sandifer on January 17, 1949. She had had

no previous illnesses of note, and on direct questioning there was no history of tetany or thyroid disorder. There was no family history of mental disturbance, epilepsy, or endocrine abnormality. The patient had had seven children. The first died in convulsion at three months, but the remaining six are well. Four years before admission it was noticed that the patient was becoming slower in her movements, and that her memory was failing. At about the same time she began to have brief attacks of vertigo, in one of which she fell forwards, cutting her head and leg; none of these attacks was associated with loss of consciousness. One year before admission her gait became unsteady, and after a further eight months her legs were so weak and unsteady that she was unable to climb stairs without assistance. Such unsteadiness of the hands as occurred did not prevent her from helping with the cooking. Attacks of vertigo, unassociated with deafness or tinnitus, occurred three or four times daily and caused frequent falls. She also complained of feelings of numbness in the tips of the fingers and of tingling in the front of the thighs. She denied impairment of memory or concentration and considered her speech to be normal. She had occasional slight frontal headaches. She had never had any fits. No change in facial expression had been noticed. Her vision was good, as was her hearing. She admitted to unsteadiness of the hands and to clumsiness and stiffness of the legs; sphincter control was normal. Her general health was good.

On examination she was seen to be a well-nourished woman with a high colour, and healthy hair, skin, and nails; there was no thyroid enlargement, and general examination revealed nothing abnormal. Her blood pressure was 135/60. Mentally she was distinctly dull, with defective insight into her condition. Her memory for recent events was impaired; she was unable to subtract serial sevens, but could retain six digits forwards, and reverse three. On the Wechsler-Bellevue verbal intelligence scale her I.Q. was 79; there was little evidence of deterioration, and it was felt unlikely that she had ever been of more than low average intelligence. There was no dysphasia, dyspraxia, or evidence of a specific defect of parietal lobe function. Speech was slow and slurred. The cranial nerves were normal except for a moderate deafness of the right ear due to

chronic otitis media; in particular, vision was good; the fields and fundi were normal and there was no cataract. The jaw-jerk was brisk, though not unduly so. There was no spontaneous tremor of the upper limbs; here tone was slightly increased and there was a little weakness of extension of the wrists. Discrete movements of the fingers were clumsy and there was a well-marked intention tremor, especially on the left. The tendon reflexes were brisk but equal; there was no grasp reflex. Sensation was normal. The abdominal reflexes were present, though sluggish. The lower limbs exhibited a moderate degree of spasticity and weakness, especially on the right side, and there was marked incoordination in the heel-knee test. The deep reflexes were very brisk, but equal, and both plantar responses were extensor. Sensation was normal.

Investigations.—A radiograph of the skull showed a calvarium of normal size and shape; the sellar region was normal. The pineal gland was faintly calcified and lay in the normal position. The caudate and lenticular nuclei on each side were heavily and symmetrically calcified, and the dentate nuclei were similarly calcified (Figs. 1a, 1b, and 2). Pneumoencephalography confirmed the position of the shadows (Figs. 3 and 4). The size of the ventricles was at the upper limit of normal, and the sulci of the frontal lobes were somewhat widened. The blood Wassermann and Kahn reactions were negative. The cerebrospinal fluid was under normal pressure, and normal in composition. The serum calcium level was normal on three occasions (9.3, 10.4, and 11 mg. per 100 ml.) and the serum phosphorus was 3.4 mg. per 100 ml. Alkaline and acid phosphatase values were normal (11.5 and 1.7 units respectively). The urine was normal. In tests for toxoplasma the complement fixation test was negative, and the cytoplasm-modifying antibody test positive 1/8.

Because there was a cholesteatomatous deposit in the attic a radical mastoidectomy was performed, after which the attacks of vertigo ceased.

Over the past two years the patient's condition has remained essentially unchanged, and the intracranial calcification has shown no increase in extent or density.

Skull radiographs of her elder daughter (L.N., aged 28) showed a mottled shadow on both sides in the position of the anterior part of the lenticular nucleus (Figs. 5a, 5b, and 6). In the case of the younger daughter (C.E., aged 21) only a very faint mottled shadow was visible (Figs. 7a, 7b). Both daughters enjoyed good health, were of average intelligence, and displayed no abnormal physical signs. Three of her four sons, aged 32, 27, and 26, were examined radiologically, and in none was any intracranial calcification visible.

Discussion

Much of the earlier work on calcification of the finer cerebral vessels in the divers conditions already mentioned was vitiated by a failure to recognize the occurrence of microscopical hyaline degeneration and calcification in the normal corpus striatum.

Mallory (1896) showed that hyaline degeneration in the media and adventitia of small vessels, with subsequent deposition of calcium salts, occurs most frequently in the dentate nucleus, and that the droplets may fuse to form sheaths. The process affects the small arteries first, later the capillaries and veins. The principal difficulty, as later workers have realized, lies in determining at what stage the process becomes pathological. In 100 brains, affected by a wide variety of pathological conditions and of all ages, Hurst (1926) found microscopical deposits in the vessels of the globus pallidus, chiefly in the small vessels of the anterior half of the nucleus, though often with sparing of the extreme rostral tip. In 68% there were free-lying, so-called degenerative bodies staining blue-black with haematoxylin (termed by earlier writers chorea corpuscles, Flechsig's granules, or siderophile bodies, and by later workers pseudolime or pseudo-calcareous concretions) in the globus pallidus, and in 30% such bodies were also to be found in the putamen. They occurred solely in the putamen in only two cases. They were also to be observed more sparsely in the internal capsule, but they have not been reported in the red nucleus, reticular substance of the midbrain or pons, or in the inferior olives. He considered that their distribution could not be entirely correlated with that of iron, for they were never to be seen in the substantia nigra. The deposits themselves are highly refractile, often laminated, devoid of lipid, glycogen and amyloid, and may be minute or sufficiently large to give a gritty feel to the knife. Ostertag's (1930) description of them accords well with that of other authors (Pick, 1902, 1903; Bassoe and Hassin, 1921; Weimann, 1922; Kasanin and Crank, 1935; Eaton, Camp, and Love, 1939; and Rand, Olsen, and Courville, 1943). They occur in three forms. They may lie free in the tissues, unrelated to the vascular system, varying in size from minute points to laminated spheres larger than a ganglion cell of the globus pallidus, or as "mulberry bodies" formed by the conglomeration of several spheres, these being encountered only in pathological conditions. Secondly, there may be deposited upon the outer side of capillaries innumerable globules, like strings of pearls, or, usually in pathological conditions, complete sheaths with or without obstruction of the lumen. Thirdly, dust-like particles and spherules may be deposited in the media, adventitia, and perivascular spaces; in the early stages they do not destroy the media or occlude the lumen, but in advanced cases they become confluent and form large, irregular, branching, coral-like masses. The deposits do not occur within glial or nerve cells, and except where vessels have become occluded

FIG. 2

FIG. 3

FIGS. 1a and 1b

FIG. 4

FIGS. 1a AND 1b.—Dense calcification in the region of the corpus striatum and dentate nuclei in Case M.E.

FIG. 2.—Half-axial view of skull. The dentate nuclei are clearly visible as sinuous shadows lying medially to the calcified lenticular nuclei.

FIG. 3.—Pneumoencephalogram to show position of calcified shadows and excess of air in subarachnoid space.

FIG. 4.—Pneumoencephalogram; reversed Townes projection.

FIGS. 5a AND 5b.—Case L.N., elder daughter of M.E. : mottled calcification in the anterior part of the corpus striatum.

FIGS. 6a AND 6b.—Case L.N. : half-axial view : no calcification is visible in the dentate nuclei.

FIGS. 7a AND 7b.—Case C.E., younger daughter of M.E. Early calcification in the anterior part of the corpus striatum.

there is no reactive gliosis. The condition is certainly not related to medial sclerosis, for the earliest deposition is often adventitial, and the subintimal tissue is the last to be affected; furthermore, in the cases reported the larger vessels at the base have always been normal. The groundwork of the deposits is a hyaline material staining as deeply with haematoxylin after decalcification as before. Debate as to whether these deposits contain iron or calcium or both has been considerable. Eaves (1926) showed that it is, in fact, calcium that is deposited in such abundance in the hyaline globules. In comparison with the amount of calcium, the quantity of iron present is small (Kasanin and Crank). Lowenthal (1948) summarized the evidence for the presence of hyaline, calcium, and iron in cases of symmetrical calcification of the corpus striatum reported up to that time.

The question arises, when may the concretions, present to some extent in the majority of brains, be regarded as abnormal? There appears to be no sharp division between the normal deposition of hyaline with its propensity for adsorbing calcium, and the abnormal as seen in the cases under discussion. The deposits in these cases are similar to those occurring in the neighbourhood of angiomatous malformations, in gliomas, at the edge of areas of necrosis, and in the familial calcifying epilepsy of Geyelin and Penfield (1929). It would appear that, so far as their appearance in the basal ganglia is concerned, these deposits may be regarded as abnormal only when they attain such a size as to become confluent and occlude vessels, causing local ischaemia and setting in train a progressive process itself tending to cause calcification.

Calcification of the Corpus Striatum and Hypoparathyroidism.—The occurrence of striking calcification in the corpus striatum in cases of tetany was noted by Pick (1902, 1903, 1905); Ostertag remarked upon the unusual density of the concretions in cretinism and mongolism. He suggested that in certain metabolic disorders excessive deposition of hyaline may occur in these regions because of some local metabolic peculiarity, with impairment of the blood supply of the ganglia and later parenchymatous damage. The particular association of radiologically demonstrable calcification in the basal ganglia with hypoparathyroidism was emphasized by Eaton and Haines (1939), Eaton, Camp, and Love (1939), Sevringhaus (1942), Mortell (1946), and Siglin, Eaton, Camp, and Haines (1947). Alexander and Tucker's (1949) case was one of the even rarer pseudo-hypoparathyroidism; this patient, who exhibited the typical habitus described by Albright (Albright and Reifenshtein, 1948), had suffered from epilepsy in adolescence; in addition to subcutaneous calcinosis (which seems to be more common in pseudo-

hypoparathyroidism than in idiopathic hypoparathyroidism) he had calcification of the basal ganglia visible radiologically. At the age of 48 he developed a typical Parkinsonian tremor. The cases of Sprague, Haines, and Power (1945) with fits and calcinosis, and of Peterman and Garvey (1948) with fits, mental retardation, and behaviour disorder, were also examples of the condition in association with pseudohypoparathyroidism. The radiological features have been reviewed by Camp (1947, 1948). With regard to other endocrine disorders, a case of Addison's disease showing concretions histologically was reported by Ostertag. The coexistence of idiopathic hypoparathyroidism with adrenal insufficiency (not due to tuberculosis) has been commented on by Leonard (1946). She reported a child in whom the two conditions occurred together, with radiologically demonstrable calcification in the basal ganglia; unfortunately the necropsy findings in the brain were not published. Maleci and Bonomini's case (1948) had in childhood suffered from adiposogenital dystrophy, and there was also a doubtful history of late rickets; in view of the raised serum phosphorus level the case may well have been one of idiopathic hypoparathyroidism. Lowenthal (1948) attempted to define the relationship between striated calcification and parathyroid insufficiency. He found that of 32 cases collected from the literature 13 in all had evidence of parathyroid insufficiency. Of these, nine had clinical tetany (two with cataract as well), and two had cataract only; the remaining two had low serum calcium and raised phosphorus levels in the absence of rickets or renal failure, but displayed no signs of tetany. Most of these cases were examples of chronic idiopathic hypoparathyroidism; in three patients it followed measles, two of these being siblings. Striated calcification is not peculiar to idiopathic hypoparathyroidism, for Scholz, quoted by Ostertag, reported a case following thyroidectomy, as did Siglin and others. It appears that a considerable time is required for the development of radiologically visible calcification after parathyroidectomy; Ostertag examined the brains of two cases of parathyroprivic tetany, dying six weeks and three months respectively after operation, and found no excess of concretions. Scholz's case came to necropsy 10 years after operation, while that of Siglin and others was radiographed 24 years after thyroidectomy.

To the 32 cases collected by Lowenthal may now, therefore, be added seven more examples with intracranial calcification: those reported by Eaves, Sevringhaus, Sprague, Mortell, Leonard, Peterman and Garvey, and Alexander and Tucker. Thus of 39 instances in the literature in which gross

calcification was demonstrated either radiologically or at necropsy, no less than 19 had undoubted parathyroid insufficiency.

Familial Examples.—Fritzsche (1935) reported a family of three siblings, two of them females, in whom radiologically demonstrable calcification of the lenticular and dentate nuclei was associated with epilepsy, oligophrenia, and, in the most severely affected, muscular rigidity. There was no clinical evidence of tetany. He considered the condition to be a heredodegeneration, though the evidence in favour of this view is not conclusive. The possibility that the condition might have been the result of an infection which had affected the whole family was not considered. It should be mentioned that radiologically and clinically there is nothing to suggest that these were cases of toxoplasmosis. The only other example of familial calcification of the basal ganglia is that of Kasanin and Crank. Their case was one of mental deterioration with progressive rigidity; a sister had a mental and physical condition similar to that of the patient but was not, unfortunately, examined radiologically; seven siblings had died in childhood; five were still alive, and all were mentally retarded. The cases which are the subject of the present report appear to be the only ones in which a hereditary dyscrasia can be postulated with reasonable certainty.

Clinical Features.—In cases of hypoparathyroidism with calcification in the corpus striatum epilepsy and mental deterioration are the rule, both beginning in childhood or early adult life, except where removal of the glands is the cause. Episodes of confusion and psychotic behaviour may punctuate the course; finally coma may ensue. With the exception of bilateral nerve deafness, cranial nerve palsies are unusual, though diplopia and ptosis have been recorded. Paraesthesiae, symmetrical or otherwise, are common and early symptoms. Of the muscular disorders, cramps, and persistent pain and stiffness in the muscles and joints, are frequent. Carpopedal spasm and positive Chvostek's and Trousseau's signs are present in only half the cases. Of the ectodermal features, cataract is the most common, together with loss of hair and coarseness of the skin. The rarer syndromes connected with hypoparathyroidism, such as myosclerosis, scleroderma with calcinosis, oesophageal spasm, and abdominal pain, have not been reported in cases showing intracranial calcification. Despite the density of the shadows in the basal ganglia, extrapyramidal symptoms and signs have in most cases been surprisingly scanty, though there is usually slowness and poverty of movement and facial expression.

In a few cases rigidity has been well marked, while one case, in whom the somatic features of pseudohypoparathyroidism were present in infancy, developed a Parkinsonian tremor at the age of 48. A slow, slurring dysarthria is common. Death occurs most often from intercurrent infection, but may result from a sudden attack of cyanosis with or without laryngeal spasm, or from raised intracranial pressure. The coexistence of epilepsy and papilloedema in cases of hypoparathyroidism without clinical tetany (Albrecht, 1924; Barr, MacBryde, and Sanders, 1938; Sutphin, Albright, and McCune, 1943; Leonard, 1946; Lyle, 1947; Berezin and Stein, 1948) is worth mentioning as it may lead to an erroneous diagnosis of cerebral tumour. The increased intracranial pressure has been attributed to cerebral oedema. Barr and others found that the calcium content of the cerebrospinal fluid of their case was normal, and suggested that the difference in concentration of calcium ions on the two sides of the haematoencephalic barrier may have been responsible for the raised intracranial pressure. Guillain, Bertrand, and Rouquès (1936) reported a case in which cramps, clinical tetany, petit mal, and generalized seizures were followed by obtundation, bilateral papilloedema, and death. The serum calcium level was 9 mg. %, and the parathyroids were histologically normal. The globus pallidus and dentate nuclei exhibited in profusion the concretions already described. In addition there was in the white matter of one frontal lobe a minute focus of demyelination surrounded by filaments and round bodies strongly suggestive of a mycotic infection.

Cases not Associated with Hypoparathyroidism.—

The clinical features of cases not associated with parathyroid insufficiency fall into two main groups. In the first, which includes the familial examples of Fritzsche and of Kasanin and Crank, mental retardation and epilepsy dating from childhood, with further deterioration in early adult life and a mixed pyramidal-extrapyramidal syndrome, have occurred. As a similar condition of oligophrenia with rigidity and epilepsy may be associated with cataract and deafness, it is not impossible that an early and transient hypoparathyroid state unrecognized in childhood, or passed off as epilepsy, may in certain susceptible individuals or families lead to progressive hyaline degeneration and calcification of vessels in the basal ganglia. A tendency to develop hypoparathyroidism may run in families; it has already been mentioned that two of the three patients with hypoparathyroidism following measles were siblings, while of five cases of hypoparathyroidism (without intracranial calcification) follow-

ing moniliasis three were siblings (Sutphin, Albright, and McCune, 1943; Albright and Reifenshtein, 1948). Moreover, pseudohypoparathyroidism has a well marked familial tendency.

The second group is less uniform, comprising Eaton, Camp, and Love's Case 3 with thyrotoxicosis and no neurological features other than the brain calcification; Case 4 with recurrent hemiplegia, and Case 5 with mental deterioration; Bassoe and Hassin's patient with unilateral convulsions, intellectual impairment, dysphasia, hemiparesis, headache, and stupor leading to death, and their second case, the only one in which the calcification was confined to one side, with contralateral hemiplegia with athetoid movements; in this girl the dentate nucleus was not calcified, and the cause may well have been a vascular accident in childhood. The subject of the present report showed intellectual impairment, slowness of movement, dysarthria, marked intention tremor in the upper limbs but no static tremor, and moderate spasticity with ataxia in the lower limbs. The affected daughters had no neurological disturbances, and there is no intracranial calcification in the sons. This incidence upon the female members of the family is interesting, and two of Fritzsche's three familial examples were females. Although in general dysfunction of the thyroid as well as of the parathyroid glands is more common in women than in men, amongst the cases of calcification of the corpus striatum reported in the literature males and females are equally represented. Whether the signs are predominantly cerebellar or predominantly extrapyramidal in the usual sense of the word presumably depends on whether the process occurs most markedly in the putamen and globus pallidus on the one hand or the dentate nucleus on the other.

Radiological Features.—There is no significant difference between the radiological features in the familial form and that associated with hypoparathyroidism. The calcification is clearly visible as multiple, dense, granular shadows, or in more advanced cases as striped or amorphous masses picking out clearly the caudate, lenticular, and dentate nuclei. The thalamus is always spared. The shadows are usually less marked in the dentate nuclei; here they may be obscured by the petrous bones, but they can be shown up clearly in half-axial projections. In half the cases a few scattered flecks of calcification are visible in the centrum semiovale or in the white matter of the frontal lobes. Calcification is not seen in the meninges, cortex, or immediate subcortical white matter. The calvarium generally shows no abnormal features. Pneumo-encephalography confirmed the

position of the calcification in eight of the 17 radiologically demonstrable cases in the literature, and in case M.E. The ventricular system was normal in all except two; in one of these there was moderate symmetrical dilatation of all the chambers, while in the other dilatation was limited to the third ventricle.

Aetiology.—Although the histopathological basis of the condition is clearly non-specific, the radiological features of all the reported cases are so similar that it is tempting to search for a common cause. The presence of hypoparathyroidism in 19 out of 39 examples is significant; yet the great majority of cases of parathyropivic tetany do not show intracranial calcification. However, nearly all the cases of hypoparathyroidism with intracranial calcification have been of the rare idiopathic variety or of the even more uncommon pseudohypoparathyroidism. It is conceivable therefore that some common factor may be responsible both for the so-called idiopathic hypoparathyroidism and for the excessive deposition of hyaline material around the vessels of the central grey matter, and that the metabolic disorder, with its tendency to supersaturation with regard to calcium and phosphorus as postulated by Albright and Reifstein, results in a superabundant deposition of calcium in the hyaline material. In one example (without striatal calcification) in the literature (Winer, 1945) a diencephalic cause of parathyroid atrophy was suggested because of localized dilatation of the third ventricle; a similar localized dilatation has been reported in one case with calcification. It is of some interest that the coexistence of parathyroid disturbance and striatal disease has been reported in two members of a family suffering from Wilson's disease of the "pseudosclerosis" type (Baltzan, 1936; Altschul and Brown, 1942). Of five siblings three had hepatolenticular degeneration, while one died young of cirrhosis. Of the former, one had hypocalcaemic tetany, but the parathyroid glands were not examined at necropsy; while the other case had displayed no tetany, but at necropsy there was moderate atrophy of the parathyroid glands. As there was also some endarteritis of the parathyroid arteries it is difficult to be certain of the relationship of the parathyroid atrophy to the hepatolenticular degeneration.

The possibility that infection might be responsible for both the hyaline degeneration and the parathyroid atrophy has been entertained. One chronic infection at least, moniliasis, has been suspected of being a cause of parathyroid atrophy; in such cases the infection precedes the metabolic disorder; furthermore, moniliasis has also been

found in two siblings with adrenal atrophy, one of whom probably had hypoparathyroidism as well (Talbot, Butler, and MacLachlan, 1943). While toxoplasmosis nearly always causes multiple small disseminated cortical and subcortical flakes and curvilinear streaks, in rare instances there may occur a dense granular or even confluent calcification of the basal ganglia (Sutton, 1951) with but few subcortical lesions. However, there is at present no evidence that this infection can disturb the function of the parathyroid glands, and in none of the cases of the condition under discussion has there been choroiditis or gross internal hydrocephalus. The strongest point against there being a single factor causing both the deposition of hyaline material in the brain and the hypoparathyroidism is the observation of calcification following accidental removal of the glands in two instances; another point is the occurrence of intracranial calcification in cases of pseudohypoparathyroidism, which appears to bear no aetiological relation to the idiopathic form. Eaton and others, and Siglin and others concluded that the intracranial calcification is indeed the direct result of the parathyroid insufficiency, but left unexplained its rarity after accidental removal of the glands. The probable explanation of this is that tetany following removal of the glands is quickly and effectively treated, while idiopathic hypoparathyroidism, masquerading as epilepsy or progressive mental deterioration, may escape treatment for years. That a chronic infection is the primary cause of the intracranial deposits is improbable, because histologically the lesions show no inflammatory changes, and in an infective process it is reasonable to expect the lesions to be disseminated at random throughout the brain. In the cases under discussion, although there are often scattered flecks of calcification in the white matter close to the basal ganglia, the heaviest calcification falls with remarkable precision within the boundaries of a physiologically related system of nuclei.

Summary

A case is reported in which dense symmetrical calcification in the caudate, lenticular, and dentate nuclei, demonstrable radiologically, was associated with intellectual impairment, ataxia, and spasticity. There was no evidence of hypoparathyroidism. Both the patient's daughters, though free of neurological symptoms and signs, exhibited similar, though less well marked, radiological changes. Calcification was not detected in three of the patient's four sons.

In half the cases reported in the literature symmetrical calcification of the dentatopallidal system

has been associated with hypoparathyroidism, almost always of the idiopathic variety.

The occurrence of hyaline degeneration and gross calcification in these physiologically related nuclei leads to the supposition that their cells have a metabolic peculiarity capable of specific derangement by a raised level of serum phosphorus or a low level of serum calcium. It is possible that a transient parathyroid insufficiency may cause a permanent, or even progressive, hyaline degeneration in and about the vessels of the basal ganglia.

There is some evidence that the process may result from certain rare chronic infections, and that such infections may affect predisposed families.

There is no radiological difference between cases with and without hypoparathyroidism, though in the latter the calcification tends to be more dense.

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Lateral and half-axial views of the skull of case M.E. have been published in "Modern Trends in Neurology", edited by Dr. Anthony Feiling (London, 1951), in the chapter on diagnostic neuroradiology by Dr. J. W. D. Bull.

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