PAPILLOEDEMA AND HYPOPARATHYROIDISM
SIMULATING BRAIN TUMOR*

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Papilloedema associated with increased intracranial pressure usually raises as the primary differential consideration the possibility of brain tumor. Once this has been eliminated for the moment by such tests as pneumoencephalography, ventriculography and angiography, a variety of etiologic factors encountered much less frequently must receive attention. One of these that has been overlooked often is hypoparathyroidism. We have found in the literature reports of 12 cases of idiopathic hypoparathyroidism with papilloedema and 20 cases of postoperative hypoparathyroidism with papilloedema. This report is of 2 instances of the latter condition. In both, the possible presence of metastasis of thyroid carcinoma to the brain was considered and in each there was found electroencephalographic abnormality though overt convulsions did not develop. The confirmation of the diagnosis was by demonstration of abnormal calcium/phosphorus levels in the serum and by reversal of the condition by therapy correcting the altered electrolytes.

CASE REPORTS

Case 1. A 25-year-old, white, right-handed housewife entered the University of California Hospital on Feb. 8, 1955, complaining of blurring of vision of the right eye and of retronasal and retrobulbar headaches of 3 weeks' duration.

Seven years before entry a subtotal thyroidectomy had been performed for the removal of "one growth that wasn't cancer;" further details were not available. At a second operation, 4 months before this present admission, carcinoma of the thyroid had been found; it was treated by total thyroidectomy and radical dissection of the neck on the left side. She was immediately placed on 2 gr. of thyroid daily.

Three days after the total thyroidectomy (October 1955) she had an episode of carpopedal spasm, relieved by intravenous, then, later, oral calcium gluconate. She stopped the latter voluntarily after taking it 1 month. Subsequently episodes of carpopedal spasm with paraesthesiae occurred whenever she became excited.

Three weeks prior to the present entry, she noted the gradual onset of intermittent retrobulbar and retronasal pain plus persistent blurring in the right lower visual

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field. The only other symptom was occasional transitory decrease in hearing for the previous 2 weeks.

Examination. The patient was emotionally tense, wept easily, and coincidentally carpopedal spasms developed which were relieved by voluntary slowing of respiration. Inflating a blood-pressure cuff about either arm caused carpal spasm and paraesthesiae within 1 minute. Percussing either cheek in the region of the main branches of the 7th nerve would cause twitching of the cheek (positive Chvostek’s sign). There was bilateral papilloedema, more on the right than on the left; neither hemorrhage nor exudate was seen. Visual fields were normal except for an enlargement of the blind spot to 12 degrees on the left and 17 degrees on the right. Visual acuity was 20/30 bilaterally. There were no lenticular opacities by slit-lamp examination.

A diagnosis of possible metastasis of thyroid carcinoma to the brain plus hypoparathyroidism was made on the basis of the history and physical examination.

Course. A roentgenogram of the chest was normal. In the basal projection of roentgenograms of the skull there was an asymmetry which was interpreted as bone destruction extending from the right petrous tip into the middle cranial fossa on that side and involving the carotid canal, the foramen ovale and the foramen spinosum. The optic foramina were normal.

Blood and urine were normal. On Feb. 16, 1955, total serum proteins were 6.8 gm. per cent, albumin 4.5 gm. per cent and globulin 2.3 gm. per cent. On that same day serum calcium was 6.0 mg. per cent and serum phosphorus was 5.6 mg. per cent. Two days later these values were 6.3 and 6.1 respectively.

On Feb. 12, 1955, burr holes and ventriculograms were carried out and on Feb. 14, 1955, a right-sided common carotid arteriogram was done. The studies were felt to be normal and did not substantiate the interpretation of the basal views of the skull mentioned above.

On Feb. 13, 1955, the spinal fluid pressure was 300 mm. of spinal fluid and the spinal fluid protein was 30 mg. per cent. Four days later the pressure was 400 mm. of spinal fluid.

An electroencephalogram, on Feb. 17, 1955, was reported by Doctor Robert B. Aird as follows:

"The resting record was characterized by alpha and beta rhythms of low and moderate voltages, which were transiently disturbed by theta activity that predominated frontally but at times involved all areas. Random slow waves of high voltage were noted on occasion in the left low frontal, central and anterior temporal regions. The record otherwise showed no clear evidence of focal pathology. The dysrhythmic activity was not exaggerated with either hyperventilation or photic stimulation. The generalized dysrhythmia would be compatible with a generalized cerebral dysfunction of convulsive or other nonspecific type."

The possibility that the papilloedema, which was becoming worse during this time, might be on the basis of hypoparathyroidism, was entertained. As a therapeutic test, treatment consisting of dihydrotachysterol, calcium lactate and Amphojel was instituted. Initially the oedema continued to advance with small hemorrhages and exudate being noted within the first 48 hours of treatment. Subsequently this subsided, however, and when the patient was last seen on April 4, 1955, the discs were characterized by secondary atrophy. Other symptoms had subsided completely. She was continuing on the therapeutic regimen under the direction of her family physician.
Case 2. A 14-year-old white, right-handed male entered the University of California Hospital on Feb. 20, 1955 for removal of a nodule of the right lobe of the thyroid, which had been found on a routine examination for insurance. There were no symptoms and a review of the past history was negative, save for polyarthritis, fever and a cardiac murmur at the age of 5 which had subsequently disappeared. The preoperative diagnosis (HHS) was carcinoma of the thyroid with metastases.

Operations. On Feb. 21, 1955, a right thyroid lobectomy was done. Adenocarcinoma of the thyroid with metastasis to the cervical lymph nodes was diagnosed and on March 21, 1955, a radical dissection of the neck was done on the right side.

Course. On the night of the 1st operation, he was found to have a questionably positive Chvostek’s sign and he was treated with dihydrotachysterol. However, the next day this sign was more marked, and tingling in the fingers was noticed. Amphojel and calcium gluconate wafers, plus a soft low-phosphorus diet were given. Calcium gluconate was given intravenously the 2nd postoperative day.

On March 22, the day after the radical dissection of the neck, a regimen of oral calcium gluconate with dihydrotachysterol, thyroid and a low-phosphorus diet was instituted. In 2 days the thyroid was increased and on the 4th postoperative day parathyroid extract was started. The positive Chvostek’s sign persisted in varying degrees throughout the entire postoperative course.

Three days after dissection of the neck the patient became drowsy and the optic discs were blurred, suggesting the development of hypoparathyroidism with increased intracranial pressure.

On the 7th postoperative day roentgen-ray therapy was started. On the 9th day there was a period of disorientation and incoherent speech. The next day bilateral abducens paresis was noticed, more on the left than right. The serum calcium at this time was 7.5 mg. per cent, and the phosphorus 6.1 mg. per cent.

Four days later decreased abdominal reflexes, absent left cremasteric reflex, intention tremor of the right arm and poorly performed heel-to-shin testing bilaterally were noted.

Fifteen days after surgery the papilloedema was more marked, particularly on the left, with fresh hemorrhages on both sides.

By April 13, 1955 (23rd postoperative day), the calcium rose to 17.4 mg. per cent and the phosphorus was 3.1 mg. per cent, presumably from overtreatment, which was appropriately changed. The patient was generally weak with markedly depressed deep tendon reflexes. Roentgen-ray therapy was interrupted but was resumed in 10 days when his symptoms improved. A central scotoma was noticed on April 27, 1955, but by May 9, 1955, the papilloedema began to improve. By May 18, 1955, there was increased power in the right arm, improved mental state and there was improvement in the weakness of the left external rectus. The calcium at that time was 9.1 mg. per cent.

He was discharged from the hospital on calcium gluconate and dihydrotachysterol but re-entered 5 days later on June 9, 1955, because of progressive visual loss. There was astereognosis of the right hand with reduced right-sided two-point discrimination and perception of figure writing. Coordinated movements of the right upper extremity were done poorly. Position and vibratory sense of the right upper extremity were markedly impaired. The right visual acuity was 20/40. There was a left-sided central scotoma. Bilateral hemorrhagic papilloedema remained more on the right. On June 13, 1955, the calcium was 10.2 mg. per cent and the phos-
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phorus 6.2 mg. per cent. The next day there was enlargement of a central and centro-cecal scotoma on the left with more papilloedema. On June 20, 1955, the cerebro-spinal fluid pressure was 350 mm.; the protein was 89 mg. per cent and the spinal fluid calcium was 4.9 mg. per cent.

The persistence of increased intracranial pressure despite a serum calcium that was within normal limits was attributed to the elevated serum phosphorus. Efforts were then made to reduce the latter by reducing phosphorus intake and by diuresis with mercurials.

Urinary excretion of phosphorus and calcium became normal and the doses of dihydrotachysterol and calcium gluconate were reduced. Potassium chloride and mercurial diuretics were continued. On June 7, 1955, the serum magnesium levels were 0.5 to 1.0 mg. per cent (normal being 1 to 3.5 mg. per cent in our laboratory). Magnesium chloride, 1 gm. four times daily, was started July 13, 1955.

All findings and symptoms slowly improved but on Aug. 12, 1955, the spinal fluid pressure remained at 340 mm. By this time the serum calcium had fallen to normal. A daily dose of 50,000 V. of vitamin D was substituted for the dihydrotachysterol. The patient continued to receive Amphojel with Benemid added.

When discharged from the hospital on Aug. 23, 1955, some improvement of the right scotoma was noticed.

At the last entry an electroencephalogram was reported by Doctor Bill Garoutte as follows:

"The wake record was disturbed by a slight generalized dysrhythmia of non-specific type, consisting of slow activity (5–7 per second frequency) and irregularity of form as well as suggestive focal changes of higher potentials, slower activity, more irregularity and poor synchrony which appeared transiently in the precentral and low frontal areas on the right. In both the wake and sleep tracings occasional isolated spiking potentials appeared in the right parietal and both temporal areas; as in the previous EEG of 7/13/55 these could not with certainty be differentiated from muscle artefact but some of them appeared to be unassociated with muscle. The findings are compatible with a mild generalized cerebral dysfunction of non-specific origin and possibly multiple irritative lesions of the cortex which raises the question of a diffuse cortical process, presumably of a degenerative nature."

When rehospitalized on Sept. 22, 1955, the patient had only slight papilloedema on the right with bilateral optic atrophy. Spinal fluid pressure was 250 mm. of spinal fluid; the protein was 82 mg. per cent.

When last seen on Feb. 19, 1956, there was no papilloedema, marked optic atrophy, slight residual sensory deficit of the right upper extremity and persistent bilateral central scotoma which were slowly improving. On Sept. 12, 1956, there was no further change in the bilateral scotoma. There had been no changes for 3 months, and he was attending school regularly.

HISTORICAL REVIEW

The first description of papilloedema associated with hypoparathyroidism which we have been able to find was by Luttwig in 1908. Albrecht found 10 previously reported cases and added 1 of his own in 1925. Shelling and Goodman in 1934 described tetany, convulsions and papilloedema in a patient after a thyroidectomy. Similar observations were made by Barr et al., Eaton and Haines and Hurxthal. Sutphin et al. in 1943 reported a
case of papilloedema associated with idiopathic hypoparathyroidism. Others have made the same observation.\textsuperscript{3,4,7,11,15,18,25,28}

Grant\textsuperscript{8} in 1933 presented 3 cases of papilloedema and convulsions after thyroidectomy. A similar combination present in 2 of 4 patients with hypoparathyroidism was reported by Sugar.\textsuperscript{26}

The reviews of this subject by Grant\textsuperscript{8} and Sugar\textsuperscript{26} include valuable discussions of other features of hypocalcemia, regardless of the cause, that are of importance to the neurologist and the neurological surgeon. Convulsions associated with hypocalcemia were reported as early as 1886 by Mikulicz.\textsuperscript{17} Electroencephalographic changes have been reported repeatedly.\textsuperscript{19} Various cerebral manifestations of hypoparathyroidism, such as confusion and excitement,\textsuperscript{20} psychosis,\textsuperscript{9} mental deterioration and retardation,\textsuperscript{2} depression,\textsuperscript{6} and delusions, hallucinations and drowsiness,\textsuperscript{22} have been reported.

Abnormalities found on neurological examination of patients with hypoparathyroidism plus papilloedema and/or seizures, include sphincter disturbances, ataxia, localized increase in deep tendon reflexes, tremors\textsuperscript{7} and choreiform movements.\textsuperscript{24}

Elevation of the cerebrospinal fluid pressure has been recorded in numerous cases, but this has not been a constant finding.

The duration of the papilloedema with tetany has varied from 3 weeks\textsuperscript{4} to 14 years.\textsuperscript{2}

As to the alterations in the level of serum calcium and phosphorus it appears that in general the former is lowered and the latter is elevated.

Spinal fluid calcium and phosphorus levels have been determined only a few times in patients with this problem and when obtained were usually normal.\textsuperscript{2,16} It would appear, therefore, that a demonstrable linear relationship between the blood and spinal fluid values of calcium and phosphorus does not always develop in the hypoparathyroid state.

It is of particular interest in Case 2 reported here that there was a persistent elevation of the serum phosphorus after fairly adequate control of the serum calcium, and only after controlling the serum phosphorus was there marked improvement in the clinical state. This suggests that the phosphorus as well as the calcium alterations may be important in causing the increased intracranial pressure.

Roberts,\textsuperscript{21} reporting the effect of parathyroid hormone upon serum levels and urinary excretion of magnesium in dogs, noted an increase in urinary excretion of magnesium. A delayed fall in urinary excretion of magnesium was followed by a rise in serum magnesium. This was attributed to renal drainage of the preparation. Parathyroidectomy in normal dogs had little effect on magnesium balance except for minor decreases in serum levels.

The 2 cases reported herein were diagnostic as well as therapeutic problems. The possibility existed that the papilloedema was caused by metastasis from proved carcinoma of the thyroid, or was related to the radical dissection of the neck with ligature of one jugular vein. We believe, however, that neither was a factor in the condition discussed.
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CONCLUSIONS

Two cases of papilloedema occurring with post-thyroidectomy hypoparathyroidism are reported.

Hyypoparathyroidism with hypocalcemia is a well established entity which has been related to the occurrence of papilloedema and increased intracranial pressure and therefore must be differentiated from other causes of this condition.

With proper therapy directed toward the hypoparathyroidism the increased intracranial pressure, papilloedema and other neurological abnormalities are reversible.

The mechanism of the increased intracranial pressure and papilloedema is poorly understood but it is possible that an elevated serum phosphorus as well as decreased serum calcium may be related to the development of the condition.

REFERENCES