Intracerebral Calcification in Central Diabetes Insipidus due to Ectopic Pinealoma: Case Report

Osamu Arisaka, Hajime Arai, Naoto Shimura, Atsuto Hosaka, Yuko Nakayama, Madoka Arisaka and Keijiro Yabuta

Departments of Pediatrics (O.A., N.S., A.H., Y.N., M.A., K.Y.) and Neurosurgery (H.A.), Juntendo University School of Medicine, Tokyo, Japan

Abstract. We report the case of a 23-year-old man who presented with late-appearing intracerebral calcification during the course of central diabetes insipidus. He had been diagnosed as having ectopic pinealoma and had received brain irradiation at the age of 11 years. Bilateral calcifications of the basal ganglia and thalamus appeared 8 years after the development of diabetes insipidus. Thereafter, the calcified lesions increased in extent on follow-up computed tomograms. Though the influence of cranial irradiation was not ruled out, the lack of evidence for any underlying metabolic defect suggested that persistent hypernatremia (hyperosmolar dehydration) due to insufficiently treated diabetes insipidus was the most probable cause of the intracerebral lesions. This has been described in previous cases of nephrogenic diabetes insipidus associated with intracerebral calcification.

Key words: intracerebral calcification, basal ganglia, central diabetes insipidus, hyperosmolar dehydration, hypernatremia

Introduction

Intracerebral calcification in children has been found in association with or as a consequence of prenatal and postnatal infections of the central nervous system, brain tumors, hemorrhage, toxic or hypoxic damage to the brain, metabolic diseases, and some congenital anomaly syndromes [1-3]. We report a rare case of concurrent central diabetes insipidus and intracerebral calcification; the calcification, revealed by computed tomography, appeared several years after the diagnosis of diabetes insipidus. To our knowledge, this association has not been previously documented.

Patient Report

A 23-year-old man, 64 kg in weight and 165.0 cm in height, was referred for evaluation of intracerebral calcification evident on computed tomography. He showed no abnormal neurological findings except for visual impairment. He worked as a masseur.
He had been diagnosed as having a suprasellar tumor by brain computed tomography at the age of 11 years, having developed polyuria and visual disturbance several months earlier. He had shown normal growth until then. On examination, he had decreased visual acuity and bilateral optic atrophy. The serum sodium concentration was 168 mmol/l. Brain irradiation 40.8 Gy was initiated immediately after the diagnosis of ectopic pinealoma had been confirmed by brain biopsy; the tumor was inoperable since the optic chiasm was involved. Computed tomograms taken over the ensuing months showed complete regression of the tumor, but the patient’s visual acuity did not recover. Examination of anterior pituitary function after irradiation revealed hypopituitarism; there was no response of growth hormone, thyroid-stimulating hormone, gonadotropins, or prolactin to combined stimulation with insulin, thyrotropin-releasing hormone and luteinizing hormone-releasing hormone. With regard to posterior pituitary function, urinary osmolarity did not increase beyond 220 mOsm/kg · H₂O after water deprivation, but it increased to 990 mOsm/kg · H₂O in response to desmopressin (DDAVP). Renal function was normal. Accordingly, the diagnosis of central (complete) diabetes insipidus was confirmed.

Hormone replacement treatment with desmopressin, thyroxine, hydrocortisone and human growth hormone was initiated soon after the cranial irradiation. Thereafter, the patient’s growth was normal, but the symptoms of polyuria and polydipsia did not subside, because of the irregular use of intranasal desmopressin resulting from his lack of skill due to visual disturbance. He preferred free access to water rather than regular desmopressin administration; however, he was eventually unable to cope adequately with dehydration, probably due to disturbed recognition of thirst. He regularly awoke once a night for urination. As shown by the data on serum electrolytes and osmolarity during the course of the disease (Table 1), the hypernatremia persisted after 11 years of age.

**Computed tomography of the brain (Fig. 1)**

Yearly computed tomographic examinations of the brain after irradiation showed no evidence of tumor regrowth. However, at the age of 19 years (8 years after irradiation), bilaterally symmetric calcification of the thalamus and basal ganglia appeared; this had not been detected on computed tomograms taken at 17 years of age. The next examination revealed that the calcified lesions had further extended and their density had increased.

**Assessment of parathyroid function**

The serum calcium, phosphate and alkaline phosphatase concentrations that had

---

**Table 1. Serum electrolytes and osmolarity during the course of diabetes insipidus**

<table>
<thead>
<tr>
<th>Chronologic age (yr)</th>
<th>11</th>
<th>12</th>
<th>13</th>
<th>14</th>
<th>15</th>
<th>16</th>
<th>17</th>
<th>18</th>
<th>19</th>
<th>20</th>
<th>21</th>
<th>22</th>
<th>23</th>
</tr>
</thead>
<tbody>
<tr>
<td>Na (135-145)*</td>
<td>168</td>
<td>147</td>
<td>159</td>
<td>155</td>
<td>160</td>
<td>154</td>
<td>161</td>
<td>155</td>
<td>158</td>
<td>159</td>
<td>156</td>
<td>162</td>
<td>166</td>
</tr>
<tr>
<td>K (3.4-5.0)*</td>
<td>3.9</td>
<td>4.0</td>
<td>3.9</td>
<td>4.1</td>
<td>4.0</td>
<td>4.2</td>
<td>4.2</td>
<td>4.0</td>
<td>3.7</td>
<td>3.8</td>
<td>3.8</td>
<td>3.5</td>
<td>3.7</td>
</tr>
<tr>
<td>Cl (96-109)*</td>
<td>120</td>
<td>107</td>
<td>119</td>
<td>116</td>
<td>115</td>
<td>119</td>
<td>115</td>
<td>115</td>
<td>121</td>
<td>118</td>
<td>122</td>
<td>122</td>
<td>125</td>
</tr>
<tr>
<td>Ca (2.1-2.5)*</td>
<td>2.2</td>
<td>2.5</td>
<td>2.3</td>
<td>2.3</td>
<td>2.2</td>
<td>2.2</td>
<td>2.4</td>
<td>2.4</td>
<td>2.4</td>
<td>2.4</td>
<td>2.5</td>
<td>2.5</td>
<td></td>
</tr>
<tr>
<td>P (0.97-1.45)*</td>
<td>1.1</td>
<td>1.3</td>
<td>1.2</td>
<td>1.5</td>
<td>1.1</td>
<td>1.4</td>
<td>1.3</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Osmolarity (285-295)**</td>
<td>299</td>
<td>319</td>
<td>336</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Serum electrolyte values are expressed as mmol/l. Normal ranges for our laboratory are indicated in parentheses. Biochemical examination was carried out three or four times a year; for each year, the data at the time when serum sodium exhibited the highest value are shown. Throughout the course of the illness, the lowest measured sodium value was 145 mmol/l.

** Actually measured (not-calculated) osmolarity is expressed as mOsm/kg · H₂O.
Cerebral Calcification in Diabetes Insipidus

Fig 1-A. Computed tomograms taken at the age of 17 years (6 years after irradiation), showing no tumor regrowth or calcified lesions. Slight brain atrophy is evident.

Fig 1-B. Computed tomograms taken at the age of 19 years, showing bilaterally symmetric calcification of the basal ganglia (left-hand tomogram) and thalamus (right).

Fig 1-C. Computed tomograms taken at the age of 23 years, showing progression of the lesions. Basal ganglia calcification has extended (left-hand tomogram) and density has increased. Bilateral periventricular calcification has newly appeared (right).
been determined during the course of the illness were, in retrospect, normal (Table 1). The circulating levels of serum intact parathyroid hormone, 25-hydroxyvitamin D and 1,25-dihydroxyvitamin D determined at the age of 23 years were all normal: 29 pg/ml (normal, 10-40), 23 ng/ml (normal, 10-55), and 66 pg/ml (normal 27-76), respectively. The Ellsworth-Howard test using 100 units of human parathyroid hormone revealed normal increases in urinary cyclic AMP and phosphate excretion (method described elsewhere [4]). A skeletal survey showed no signs of Albright’s osteodystrophy [5].

Discussion

To our knowledge, intracerebral calcification has not been reported previously as a complication of central diabetes insipidus [6]. However, children with nephrogenic diabetes insipidus (NDI) associated with intracranial lesions (bilaterally symmetric calcification of the cerebral cortex and/or basal ganglia) have been documented [7-11]. In such patients with NDI, the pathogenesis of calcification has been thought to be calcium deposition within and/or around the walls of vessels caused by recurrent severe hyperosmolar dehydration [3, 9-12].

In considering the possible pathogenesis of the intracerebral calcification in the present patient, a late irradiation effect cannot be ruled out. Irradiation-associated calcification has been documented [1-3, 13]. Arterioles and capillaries are sensitive to irradiation, which can result in fibrinoid necrosis of the vessel walls and subsequent calcification [3]. However, the mode of calcification observed in the present patient, which showed bilaterally symmetrical extension, suggests a metabolic pathogenesis rather than a residual effect of irradiation. Any underlying metabolic disease causing calcification of the basal ganglia, including all forms of hypo- and pseudohypoparathyroidism [4, 5], was ruled out by the data on parathyroid function and by the roentgenological examination of the skeletal system. A congenital anomaly associated with calcification, or intrauterine infection leading to intracranial calcification, was also ruled out, because the lesion was not detected by the initial computed tomographic examination at the age of 11 years.

This patient with central diabetes insipidus due to ectopic pinealoma manifested persistent hypernatremia for a number of years. In general, relatively normal osmolarity can be maintained in patients with diabetes insipidus who have normal recognition of thirst [6]. The unusual persistent hypernatremia in this patient may have been associated with irregular use of nasal desmopressin and inability to sense thirst in response to increased osmolarity due to damage of the hypothalamic thirst center. In any event, the persistent hyperosmolar state was thought to have been responsible for the development of intracerebral calcification.

We were able to observe the progression of the intracranial lesions in the patient from before the calcification had appeared. Such serial observations have not been documented in other cases of NDI associated with intracerebral calcification [6-10]. Although the irradiation may have increased the susceptibility of the brain tissues to hyperosmolarity, we think that this case strengthens the view that persistent hyperosmolar dehydration, as in NDI, leads to intracerebral calcification.

Acknowledgment

The authors thank Professor H. Kuru, MD, Department of Radiology, Juntendo University School of Medicine, for assessing the brain computed tomograms.

References

Cerebral Calcification in Diabetes Insipidus