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## Adrenal crisis provoked by dental infection: case report and review of the literature

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Primary adrenal insufficiency is an endocrine disorder characterized by cortisol and aldosterone deficiency caused by destruction of the adrenal cortex. Adrenal crisis is a medical emergency with acute symptoms: nausea, vomiting, abdominal pain, fever, hypoglycemia, seizures, hypovolemic shock, and cardiovascular failure. It occurs in patients with chronic adrenal insufficiency who are exposed to additional stress, such as infection, trauma, or surgical procedures. Dental infection is a possible cause of adrenal crisis in patients with chronic adrenal insufficiency, so pediatric endocrinologists and pediatric dentists should be aware of this risk. The purpose of this report was to present a 6-year-old patient in whom Addison disease was diagnosed through adrenal crisis provoked by dental infection. The patient was treated with intravenous rehydration, intravenous hydrocortisone and antibiotics, and extraction of the infected primary tooth. Multidisciplinary approach and collaboration between the pediatric endocrinologist and the pediatric dentist are necessary to enable adequate medical and dental treatment in children with primary adrenal insufficiency. (*Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2010;110:325-329)

Primary adrenal insufficiency is an endocrine disorder characterized by cortisol and aldosterone deficiency caused by destruction of the adrenal cortex.<sup>1,2</sup> Addison disease encompasses all forms of acquired primary adrenocortical insufficiency. The most commonly recognized etiologic factor is autoimmune adrenalitis, followed by adrenoleukodystrophy, infection, bilateral adrenal hemorrhage, adrenal tumors, adrenalectomy, and drugs.<sup>1-4</sup> Clinical presentation occurs when there has been a loss of >90% of both adrenal cortices. Concomitantly, the progression of the disease is usually slow,

and typical clinical findings of weakness, fatigue, anorexia, weight loss, and skin hyperpigmentation can be very subtle.<sup>1-3,5</sup> Because gradual adrenocortical destruction diminishes adrenal reserve, the basal steroid secretion may be normal, but because secretion does not increase in response to stress, acute adrenal crisis can be precipitated by stress, such as infection, trauma, or surgical procedures in previously untreated patients.<sup>6</sup>

Adrenal crisis is a rare life-threatening condition resulting from acute adrenal insufficiency. It often occurs as an acute illness in patients with chronic adrenal insufficiency who are exposed to additional stress, i.e., infection, trauma, or surgical procedures.<sup>7-9</sup> Clinical presentation includes sudden onset of symptoms such as nausea, vomiting, abdominal pain, fever, hypoglycemia with consequent seizures, hypovolemic shock, and cardiovascular failure which may result in severe morbidity and mortality if treatment is delayed.<sup>10-14</sup> Treatment includes immediate administration of glucocorticoids, fluid and electrolyte restitution, life-long glucocorticoid and mineralocorticoid replacement, and treatment of the event or the condition that precipitated the crisis.<sup>10,15,16</sup>

There are numerous publications regarding recommendations for preventing adrenal crisis in dentistry.<sup>4,17-27</sup> Several publications describe cases of dental patients with adrenal insufficiency and acute adrenal insufficiency in response to dental procedure. Scheitler et al.<sup>28</sup> described response to tooth extraction in a patient with

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Fig. 1. Hyperpigmentation of skin folds.

adrenal insufficiency, Broutsas and Seldin<sup>29</sup> described adrenal crisis in a dental patient after tooth extraction, Cawson and James<sup>30</sup> described a case of adrenal crisis in a patient on systemic corticosteroid therapy, and Aono et al.<sup>7</sup> described onset of adrenal crisis during examination in a patient before maxillofacial surgery. However, no paper describing dental infection as the only cause could be found in either medical or dental literature. The purpose of the present report was to present a patient in whom Addison disease was diagnosed through adrenal crisis provoked by dental infection.

### CASE REPORT

A 6-year-old boy was referred to the Intensive Care Unit of the “Dr. Vukan Cupic” Mother and Child Health Care Institute of Serbia owing to toxic appearance, fever, and malaise accompanied by diminished appetite and sense of thirst. Patient presented with confusion, fatigue, and fever (41.0°C), and he was hypotensive (90/60 mm Hg), with increased heart rate (110 bpm) and respiratory rate (24 bpm). The day before admission, he had a toothache, swelling of the right cheek, high fever, and orthostatic symptoms. During last 3 years, his parents noticed general fatigue and darker skin tone. He also had a craving for salty food during the preceding months. Otherwise, his medical and dental history was unremarkable.

Physical examination showed that the boy was underweight (body mass index for age and gender was below the third percentile) and had general skin hyperpigmentation, with marked hyperpigmentations in the area of skin folds and scar tissue (Fig. 1). Extraoral examination revealed swelling of the right cheek which was 4 cm in diameter, solid, and painful on palpation. The skin above the swelling did not exhibit increased local surface temperature or redness. The parents reported that the swelling had rapid onset and progression. The boy had trismus with maximum vertical dimension measuring 25 mm. Intraoral examination revealed gin-



Fig. 2. Gingival hyperpigmentation observed during dental examination.



Fig. 3. Intraoral appearance of the infected tooth: primary mandibular second molar on the right side.

gival hyperpigmentation (Fig. 2) and the full complement of primary dentition with 1 filled tooth and 6 decayed teeth. The right mandibular second molar was grossly decayed and responded painfully to vertical percussion and palpation of the apical region (Fig. 3). The retroalveolar radiography of the right mandibular second molar revealed radiolucencies associated with the periradicular region of the affected primary tooth (Fig. 4). The findings from extraoral, intraoral and radiographic examination and caries removal confirmed the diagnosis of apical periodontitis in a primary right mandibular second molar.

Laboratory investigations revealed elevated erythrocyte sedimentation rate (40 mm/h) and C-reactive protein (53.1



Fig. 4. Retroalveolar radiograph of the right mandibular second molar.

mg/L), marked hyponatremia (123 mmol/L), hypernatruria (132.0 mmol/L), compensated metabolic acidosis (pH 7.373,  $p\text{CO}_2$  30.0 mm Hg,  $p\text{O}_2$  25.6 mm Hg,  $\text{HCO}_3^-$  17.1 mmol/L, actual base excess  $-6.9$  mmol/L, and standard base excess  $-7.2$  mmol/L), low serum aldosterone level (2.4 ng/dL), and very low level of plasma cortisol with no increase in plasma cortisol level after corticotropin stimulation test ( $<10$  nmol/L). Results of a complete blood count were white blood cells  $9.7 \times 10^9/\text{L}$  (84.8% granulocytes, 12.9% lymphocytes and 2.3% monocytes), platelets  $220 \times 10^9/\text{L}$ , hemoglobin 93 g/L, red blood cells  $3.71 \times 10^{12}/\text{L}$ , mean corpuscular volume 78.8 fL, and hematocrit 0.29. The patient's medical history, examination, and laboratory findings in the context of the sudden onset of high fever, nausea, anorexia, weakness, confusion, orthostatic hypotensive symptoms and general toxic appearance confirmed that the boy was admitted in the acute state of adrenocortical insufficiency—adrenal crisis provoked by dental infection.

The patient received intravenous hydrocortisone (10 mg/m<sup>2</sup> body surface area per day) and was parenterally rehydrated. Because of persistent fever, high levels of inflammatory markers, and lack of response to first-line antibiotic therapy, broad-spectrum parenteral antibiotics were administered (amikacin 15 mg/kg/d, ceftriaxone 100 mg/kg/d, and metronidazole 30 mg/kg/d). On the 14th day of hospitalization, the patient was premedicated with 25 mg hydrocortisone acetate given intramuscularly 1 hour before dental treatment and referred to the Department of Pediatric and Preventive Dentistry, Faculty of Dentistry, University of Belgrade, where the right primary mandibular molar was extracted (Fig. 5).

Immediately after the patient was stabilized, necessary preventive measures and dental treatment of the remaining decayed teeth were performed.



Fig. 5. Extracted infected primary tooth with visible apical lesions.

## DISCUSSION

Adrenal crisis is a medical emergency.<sup>12,14</sup> Differential diagnoses include severe acute infections, acute abdomen, various disturbances of the central nervous system, and acute poisoning.<sup>1,2,8,12</sup> In the present case, the laboratory findings of hyponatremia, hypernatruria, low serum aldosterone and cortisol levels, and lack of cortisol response to corticotropin stimulation test confirmed the diagnosis of acute adrenocortical insufficiency previously established based on the patient's medical history and examination findings and excluded other differential diagnoses.

Tissue destruction due to acute infection and emotional stress causes 3-15 times higher cortisol excretion in a person with normal adrenal function.<sup>1</sup> Gradual adrenocortical destruction decreases adrenal reserve in patients with acquired primary adrenal insufficiency. Therefore, the major risk to the patient with primary adrenal insufficiency is the lack of normal serum cortisol response to stress and of a normal renin-angiotensin response to hypovolemia, so that refractory shock may occur. The exact mechanism of cortisol response to stress is not completely understood. It has been observed that without higher cortisol serum levels during stress, the vascular smooth muscles become less responsive to circulating epinephrine, which causes capillaries to dilate and become more permeable. These effects impair vascular compensation for hypovolemia and promote vascular collapse.<sup>31</sup> Compared with adults, children are more susceptible to organ hypoperfusion, owing to increased resting metabolic rate and increased insensi-

ble water loss which makes them even more at risk for the severe presentation and complications of acute adrenocortical insufficiency.<sup>32</sup>

Thus, acute adrenal crisis can be precipitated by stress such as dental treatment or dental infection. In untreated patients, preexisting symptoms would be intensified, as resulted in the present patient. In a patient with primary adrenal insufficiency, this type of body response to stress must be reproduced by "stress coverage," meaning additional steroid administration to prevent adrenal crisis.

In the present case, the absence of fluctuation and severe pain suggested subperiosteal localization of dental abscess. Any dental abscess has the potential to become a life-threatening situation, especially if the patient is already compromised with a systemic disease such as primary adrenal insufficiency. Adrenal crisis requires immediate medical treatment consisting of intravenous glucocorticoid administration, fluid and electrolyte replacement, and treatment of the event or the condition that provoked the crisis, in this case dental treatment of the infected tooth. According to the literature, antibiotic therapy is not prescribed if the dental infection is contained within the pulpal tissue or the immediately surrounding tissues, i.e., if the patient has no signs of systemic involvement, namely, no fever.<sup>33,34</sup> Because of persistent fever, high levels of inflammatory markers, and lack of response to first-line antibiotics, broad-spectrum parenteral antibiotics were administered to our patient. Detailed pain history in this patient revealed unstimulated pain that could not be relieved by analgesics and decreased as soon as an abscess has been formed. This indicated advanced irreversible pulp damage, and therefore drainage as a treatment procedure could be considered. However, as it is almost impossible to achieve adequate drainage through a primary tooth, the only proper avenue of definitive treatment in this case was extraction.<sup>34-36</sup> Immediately after the patient was stabilized, extraction of the infected tooth with adequate premedication with hydrocortisone was necessary to enable definite treatment and to avoid precipitation of repeated adrenal crisis.

Children with primary adrenal insufficiency are high-risk dental patients.<sup>4</sup> Dental treatment using current management model may initiate psychologic and physical stress in children. Therefore, dental treatment of a patient with primary adrenal insufficiency should include behavioral principles and focus on the avoidance of physical and psychologic stressors. In cases when primary adrenal insufficiency is already diagnosed, the dentist should obtain a comprehensive medical history and consult with the endocrinologist, owing to necessary premedication regarding the type and extent of

dental treatment needed. Recommended stress dosing regimen in adult patients with chronic adrenal insufficiency undergoing major oral surgery consists of 50-100 mg/d hydrocortisone before surgery and during the first day after surgery. For adult patients in the moderate risk category (minor oral and periodontal surgery), recommended steroid supplementation is a single 25-mg dose of hydrocortisone before surgery, and no increase in steroid dose is required for patients undergoing routine nonsurgical dental treatment under local anesthesia.<sup>4,20</sup> However, more precise adjustment of steroid dose increase is needed for stress-dosing of pediatric patients. Mild stresses, such as routine nonsurgical dental treatment under local anesthesia may not require use of a stress-dose steroid regimen if the patient otherwise acts and appears well. Moderate stresses, such as minor oral and periodontal surgery, require increased doses, with 30-50 mg/m<sup>2</sup> hydrocortisone (approximately tripled daily dose) divided into 3 or 4 doses over 24 hours. Severe stresses, as in children and adolescents undergoing major oral surgery, should be treated with higher doses of hydrocortisone, up to 100 mg/m<sup>2</sup> divided into 4 doses over the day intravenously. In most cases, increased doses should be administered only during 24-48 hours, unless the underlying condition is prolonged.<sup>34,37</sup> In the present case, primary adrenal insufficiency was discovered when adrenal crisis occurred. Because dental infection is a possible cause of adrenal crisis in patients with chronic adrenal insufficiency, pediatricians and pediatric dentists should be aware of this possibility, the differential diagnosis, and adequate treatment.

## CONCLUSION

Pediatricians and dental practitioners should be aware of possible adrenal crisis due to dental infection and of necessary identification of risks in dentistry. Further efforts should be based on constant improvement of oral health in children with primary adrenal insufficiency. Regular dental examinations, comprehensive preventive measures, and timely treatment enable improvement of both oral and general health and consequently better quality of life in this high-risk subpopulation of children. Therefore, multidisciplinary approach and collaboration between pediatric endocrinologist and pediatric dentist is necessary to enable definitive treatment and eliminate underlying dental condition provoking the crisis.

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