# III. PEDIATRICS

# EMPTY SELLA SYNDROME A CAUSE FOR GROWTH HORMONE DEFICIENCY (GHD) OR JUST A COINCIDENT ASSOCIATION?

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**Abstract**

The paper aims to establish a corelation between the computer tomographic finding of Empty Sella Syndrome and the growth hormone deficit (GHD) in children. The authors present 20 children with GHD evaluated and followed up in Clinic II Pediatrics Timişoara. The complete evaluation of children for GHD at diagnosis included, besides other investigations, hormonal dosage of GH and CT imaging of the pituitary. The study raises a question upon the involvement of the radiological empty sella syndrome in causing GHD, as the syndrome may represent the cause for the GHD in children but it may also be a coincident association with it.

**Key words:** empty sella syndrome, growth hormone deficit, computer tomography

**Background**

The empty sella syndrome occurs when the subarachnoid space extends into the sella turcica, partially filling it with cerebrospinal liquid. This process causes the remodeling and enlargement of the sella and also the compression and flattening of the pituitary. Thus, it is a morphological finding consisting in a descending of the arachnoid into the sella, so that the anterior pituitary tissue may not be seen (1,2).

Primary empty sella, resulting from a congenital incompetence of the diaphragma sellae, is most frequent in children, while the secondary form (after radiotherapy, surgery) is usually found in adults. The diagnosis is confirmed by computer tomography (CT) or magnetic resonance imaging (MRI) of the hypothalamic-pituitary region, showing more than 4 mm air or liquid above the diaphragmatic line, leaving most of the sellar cavity empty (1,3).

This radiological abnormality may be associated with deficiencies of anterior pituitary hormones including the growth hormone deficit (GHD), but may also be found accidentally coexisting with a normal pituitary function (4).

The authors tried to evaluate the frequency of empty sella syndrome (ESS) and its relationship with the growth hormone deficiency (GHD) in the child.

**Material and method**

We studied 20 children (13 males and 7 females) aged between 5 $^{6}/_{12}$-16 years admitted in Clinic II Pediatrics Timisoara for short stature and diagnosed with GHD after a complex clinical and biological evaluation.

The diagnostic criteria for GHD included:

- Clinical and auxological criteria
  - short stature (height more than 3SD below the mean for age and sex);
  - decreased growth velocity (< 25$^{th}$ percentile for age and sex);
  - delayed bone age;
- subnormal GH response at two provocative tests (RIA method). We used the GH stimulation test with intravenous insulin (0,1-0,15 i.u./kg) and considered a GHD at cut-off level of 3 ng/ml (total GHD) and 7 ng/ml (partial GHD).

Besides the investigations mentioned, a complete set of usual laboratory evaluation was performed in all cases and, also, some specific investigations (hormonal dosages) in selected cases:
- thyroid hormones (TSH, FT4, TT4, TT3);
- serum cortisol;
- serum prolactin;
- gonadotropins and sex steroids – in pubertal patients.

The imagistic evaluation of the pituitary consisted in:
- Radiography of the sella turcica;
- CT scan of the hypothalamic pituitary region.

**Results**

All children were diagnosed with GHD according to the clinical, auxological and hormonal evaluation. Depending on the GH peak at the insulin tolerance test, we found 11 patients with total GHD and 9 patients with partial GHD; 9 of 20 (45%) patients with GHD, were diagnosed with primary empty sella syndrome on CT scan (no history of cranial trauma, infection or radiation was revealed).

None of the subjects presented any modifications of the sella turcica on the standard cranial radiography.

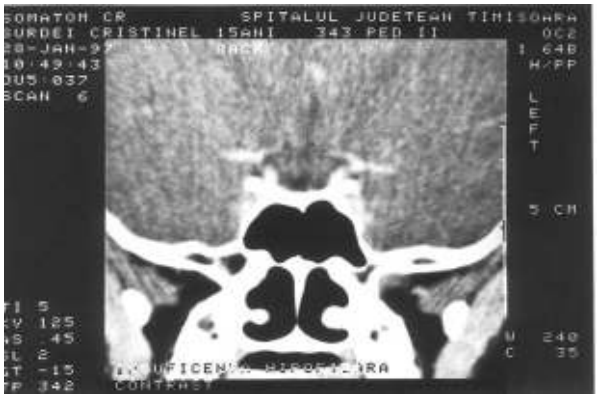


Fig nr.1. CT scan – Empty Sella Syndrome y empty sella syndrome depending on gender, revealed a predominance of males (6 cases) with a sex ratio of 2/1 = male/female. Analyzing the relationship between the empty sella syndrome and the peak of growth hormone after stimulation, of the 9 patients with empty sella syndrome we found 8 patients with total GHD (peak GH below 3 ng/ml) and 1 patient with partial GHD.

The patients showing normal aspect of the hypothalamic pituitary region at the CT evaluation (11 cases) presented total GHD in 3 cases and partial GHD in 8 cases.

**Discussions**

The literature data mention that this radiological abnormality due to an incompetent sellar diaphragm, may be associated with deficiencies of the anterior pituitary hormones but when found as an incidental finding, it is most likely that normal pituitary function will be demonstrated (4,5,6,7). Also, it is mentioned that the syndrome is more frequently associated with hypothalamic pituitary abnormalities in childhood than in adult (8).

This entity was found in our patients on the occasion of the imagistic CT evaluation of hypothalamic pituitary region for the suspicion of growth hormone deficiency.

Keeping in mind the etiology of the syndrome, we presume that the compression of the somatotrophic cells by the arahnoidocel might be able to induce a cellular dysfunction leading to a decrease in the GH secretion. Some other studies that have also found an association between empty sella syndrome and growth hormone or other pituitary hormone deficits (7, 8) sustain our hypothesis.

We consider that the growth hormone deficiency could be the consequence of the empty sella syndrome as much as it may also be a simple coincident association. The finding of 11 cases with normal CT aspect, along with 9 patients with empty sella syndrome between the 20 GHD children investigated, sustains this hypothesis. Also our results showing the association of total GHD in 8 of 9 cases of empty sella syndrome, sustain the possible involvement of the syndrome in the etiopathogenesis of GHD. The relation remains hypothetical for the moment.

Anyway, the relatively high frequency of the association between the empty sella syndrome and the GHD - resulting from our study - raises a question sign concerning the involvement of the syndrome in the pathogenesis of GHD in the child.

All cases benefited of substitutive treatment with recombinant growth hormone (rhGH) (Norditropin and later Norditropin SimpleXx, Novo Nordisk A/S) 0,025-0,035 mg/kg/day, administered daily, at bedtime. The outcomes of the treatment were comparable with those mentioned in the literature.

**Conclusions**

1. Although classically the ESS has been rarely mentioned as a cause for clinical manifestations or abnormal tests of the anterior pituitary function, our study shows that the syndrome seems to be quite frequent in the children with GHD.
2. The CT or MRI evaluation of the hypothalamic pituitary region should be performed in all children with growth hormone or other pituitary deficiencies.
3. Remains uncertain if the empty sella syndrome represents the cause for the GH deficiency in our patients or is just a pure association with it, as long as we couldn` t find any other cause for the GH deficiency.

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