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Pituitary Stem Interruption Syndrome and Celiac Disease: When Endocrinopathy and Autoimmunity Meet

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Abstract:
Pituitary stem interruption syndrome (PSI) is a rare and severe congenital anomaly characterized by pituitary insufficiency of structural origin. Clinically, SITP often manifests itself in childhood as an isolated statural growth retardation associated with growth hormone deficiency, but may also involve other hormonal deficiencies, depending on the severity of the involvement.
Furthermore, recent studies suggest an interconnection between SITP and certain autoimmune diseases, such as celiac disease, an autoimmune enteropathy triggered by gluten. This association, although rare, illustrates the complex interactions between the endocrine and immune axes, underlining the importance of multidisciplinary clinical exploration in the diagnosis and management of patients. This article provides an in-depth analysis of this association, focusing on its diagnosis, therapeutic implications, and potential relationship with other autoimmune conditions.

Keywords: Pituitary stem interruption syndrome (PSI), Statural delay, Celiac disease, Autoimmune diseases

Résumé :
Le syndrome d'interruption de la tige pituitaire (PSI) est une anomalie congénitale rare et grave caractérisée par une insuffisance hypophysaire d'origine structurelle. Cliniquement, le SITP se manifeste souvent dans l'enfance comme un retard de croissance statural isolé associé à une carence en hormone de croissance, mais peut aussi impliquer d'autres carences hormonales, selon la sévérité de l'atteinte.
De plus, des études récentes suggèrent une interconnexion entre le SITP et certaines maladies auto-immunes, comme la maladie cœliaque, une entéropathie auto-immune déclenchée par le gluten. Cette association, bien que rare, illustre les interactions complexes entre les axes endocrinien et immunitaire, soulignant l'importance de l'exploration clinique multidisciplinaire dans le diagnostic et la prise en charge des patients. Cet article présente une analyse approfondie de cette association, en mettant l'accent sur son diagnostic, ses implications thérapeutiques et sa relation potentielle avec d'autres maladies auto-immunes.
Mots clés : Syndrome d'interruption hypophysaire (PITS), retard statural, maladie cœliaque, maladies auto-immunes

Introduction:

Pituitary stem interruption syndrome (PSI) is a rare but serious congenital anomaly characterized by pitui-

tary insufficiency. The condition results from abnormal development of the pituitary stalk and associated pituitary structures, observable on medical imaging (MRI) [1]. The pathology manifests itself mainly in childhood, often as an isolated statural retardation, which is one of the first detectable clinical signs. This stunting is due to a hormonal deficiency, notably in growth hormone (GH), but may also be associated with other endocrine deficits, depending on the case.

Dysfunction of the hypothalamic-pituitary axis, involved in the regulation of hormones necessary for growth and metabolism, can have major clinical consequences if not promptly diagnosed and treated. Although SITP is mainly considered an endocrine pathology, recent studies have highlighted its possible association with autoimmune diseases, such as celiac disease. Celiac disease, a systemic autoimmune disorder triggered by gluten consumption in genetically predisposed individuals, is frequently associated with these disorders. This correlation is based on a common genetic predisposition, notably the HLA-DQ2 and HLA-DQ8 haplotypes, which predispose patients to certain endocrine pathologies [2 3].

Because of this variety of associations, regular screening for endocrine disorders is recommended in celiac patients, in order to prevent long-term complications and tailor management optimally. A multidisciplinary approach involving endocrinologists, gastroenterologists and pediatricians is essential to improve patient prognosis.

Materials and methods:

We report the case of two patients followed in pediatric endocrinology and pediatric gastrology consultation for growth retardation; perfectly illustrating this dilemma between two completely different conditions, but which may overlap in certain circumstances in the presence of a real permanent statural deficiency.

Results:

Patient A, 15 years old and male, was referred for persistent severe growth retardation accompanied by physical and psychic asthenia, with a history of celiac disease since the age of 6. Clinically, he presented with severe statural retardation (-4.5 DS) and underweight retardation (-4 DS), associated with a dysmorphic syndrome, a childlike voice, delayed puberty (stage P1G1), a 2/1 cm micropenis (-3 DS) and bilateral cryptorchidism. (Table 1)

Patient B is a 9-year-old girl referred for growth retardation accompanied by physical and psychological asthenia. Her history included celiac disease and allergy to cow's milk protein, on an adapted diet. On clinical examination, she presented with stunted stature (-3 DS) and weight (-4 DS), a dysmorphic syndrome and achromic skin lesions. (Table 1)

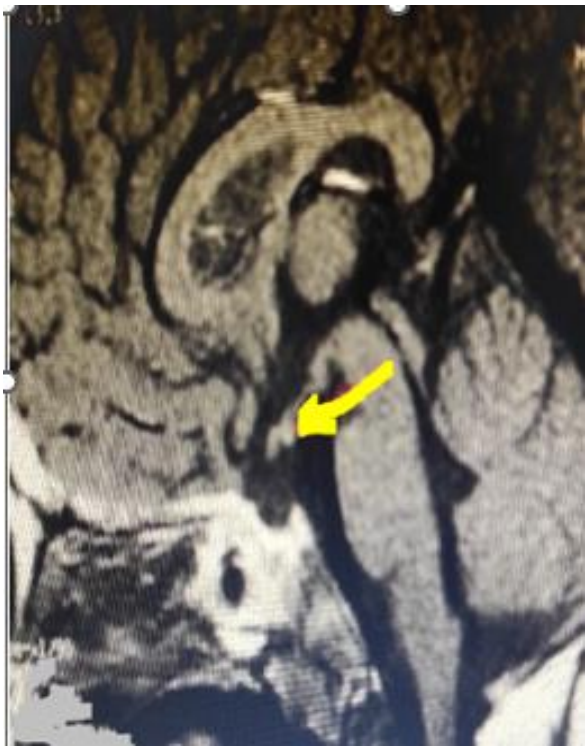

Figure 1: Invisible pituitary stem, hypoplastic anterhypophysis with ectopic posthypophysis behind the optic chiasm.

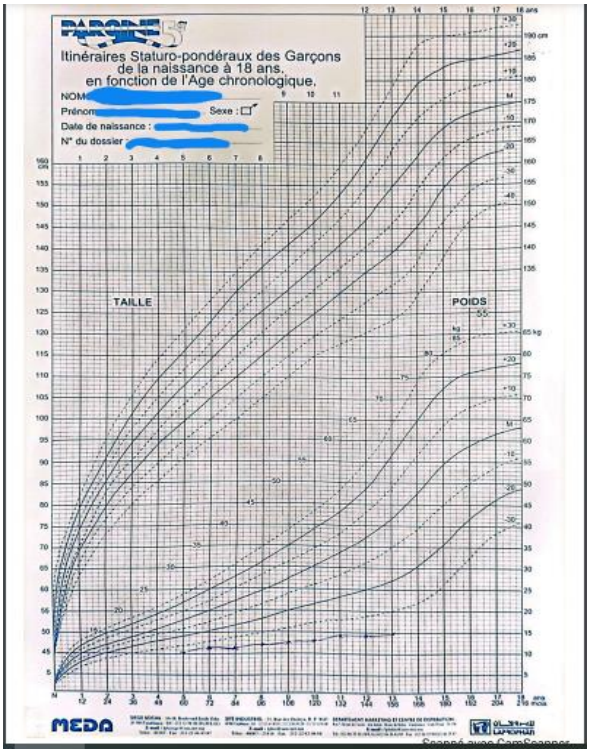

Figure 2: A growth curve showing severe retardation at -4DS.

	Patient A	**Patient** B
Age	15 years old	9 years old
Sex	M	F
ATCD	History of celiac disease since age 6, on gluten-free	Celiac disease and cow's milk protein allergy on a diet
Para-clinical exam	Pituitary somatotropic, thyrotropic, gonadotropic and corticotropic deficiency Pituitary MRI: pituitary atrophy, pituitary stalk non-individualizable (Figure 1) -Bone age: 13.5 years	- pseudo-hypoparathyroidism with GH deficiency -MRI showing pituitary disruption syndrome
Prise en ch Treatment arge	Mise sous traitement par hormone de croissance.	Treatment with growth hormone.
Evolution	Height and weight gain	poor staturo-ponderal evolution

Table 1: Clinical, paraclinical and therapeutic aspects of patients with celiac disease and pituitary disruption syndrome.

Discussion:

The two cases described present features of pituitary stem interruption syndrome (PSI), with multiple pituitary deficits. This syndrome is well reported in the literature, notably in a review of 27 cases, which emphasizes that this syndrome frequently results in severe growth retardation (-2 to -4 DS) and is associated with structural abnormalities of the pituitary gland visible on MRI, such as an interrupted pituitary stalk and an ectopic post-hypophysis. These features are consistent with our observations (statural delay and MRI abnormalities) [3].

A case study (Bordeaux thesis) also highlights the etiological heterogeneity of SITP, involving congenital causes, sometimes associated with midline malformations, or post-traumatic events. The two patients presented in our article show several deficits with a variable response to hormonal polysubstitution, which also reflects the contrasting response observed in our cases.

The pathogenesis responsible for short stature in celiac disease is still poorly understood, and is often attributed to generalized or selective malnutrition. Restricting gluten from the diet is the most effective treatment. It leads to rapid and maximal recovery of growth during the first year of treatment [3]. Thus, if there is no gain in height or a slow rate of growth after starting a gluten-free diet, other associated disorders should be considered, notably endocrine abnormalities such as GH deficiency, especially if there are signs pointing to other pituitary abnormalities, notably the severe growth retardation and signs of hypothalamic-pituitary involvement of the 2 cases reported. Brain imaging should be requested in patients with celiac disease who after a gluten-free diet for at least 1 year, despite seronegativity of serum markers, particularly anti-endomysium antibodies [2].

Furthermore, in these patients with celiac disease and pituitary stalk interruption syndrome, pituitary deficits are often associated, with morphological abnormalities of the hypothalamo-pituitary region always present as pituitary stalk interruption.

Furthermore, Bozzola et al (2005) report that combined treatment with a gluten-free diet and growth hormone can be effective in improving growth in these patients. In our observations, patient A benefited from this type of management with a satisfactory statural and weight gain, unlike patient B, who shows an unfavorable evolution despite treatment, possibly due to complex comorbidities.

The most frequent association is with type 1 diabetes, observed in 4-10% of patients with this disease.

Both conditions share autoimmune mechanisms and require close monitoring, particularly in cases where gastrointestinal symptoms or growth retardation are observed. In addition, autoimmune thyroid diseases, such as Hashimoto's thyroiditis or Graves' disease, are also common in coeliac patients, with a prevalence of up to 10-30%. Less frequent associations include autoimmune adrenal insufficiency (Addison's disease), although this remains rare, and autoimmune hypoparathyroidism, which may form part of autoimmune polyendocrine syndromes. These disorders require early diagnosis to avoid the serious complications associated with hormone deficiencies. [4]

Conclusion:

Pituitary stem interruption syndrome is a major etiology of endocrine-induced stunting, requiring in-depth exploration of the hypothalamic-pituitary axes. At the same time, celiac disease, through its autoimmune mechanism, can also contribute to growth retardation, sometimes in association with other systemic pathologies. The potential coexistence of these two conditions, or of other associated conditions, underlines the importance of multidisciplinary management and longitudinal follow-up. An integrative diagnostic strategy, combining endocrine exploration and screening for autoimmune diseases, is essential to elucidate the underlying mechanisms and ensure early and appropriate therapeutic intervention.

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