# Unsuspected malabsorption as a cause of severe acute hypocalcemia in a treated-autoimmune hypoparathyroidism (APS1)

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## APECED syndrome

**Autoimmune polyendocrinopathy type 1** (APS1), or APECED syndrome, is a **rare** autosomal recessive genetic disease. Autoimmune **hypoparathyroidism** is usually the first clinical manifestation and the most prevalent. Other manifestations of the disease are classically chronic mucocutaneous candidiasis and adrenal insufficiency.
**Treatment** will depend on the affected organ and could be challenging throughout life, especially because of development of combination of different auto-immune disorders.

## Case report

### Introduction

**A 22-year-old woman** was admitted to the emergency department for **severe acute hypocalcemia**. She was diagnosed for **hypoparathyroidism** at the age of 4 after seizure caused by hypocalcemia. At 14-year-old, she developed an **ovarian failure**. At that time, APS1 was confirmed by molecular analysis: homozygous mutation in exon 6 of *AIRE* gene [c.798del (p.Gly267ValfsX111)]. Puberty was induced by estradiol transdermal patch, later replaced by a pill of Déso 30®. She had also a **history** of vitiligo and asthma treated by leukotriene receptor antagonist.
Serum calcium was stable over time under oral calcium (1.5 g/day) and calcitriol (0.75 µg/day). However, she developped nephrolithiasis three years before admission.
Despite persistent adherence to the treatment, she developped **severe acute hypocalcemia** (corrected serum calcium 1.3 mmol/L). In addition to hypocalcemia related-tetany, she complained of **abdominal pain** and **diarrhea**. Acute **treatment** was initiated with intravenous administration of calcium gluconate. Persisting hypocalcemia required increased oral doses of calcium (4 g/day) and calcitriol (2 µg/day).
1,25-dihydroxy-vitamin D raised slightly despite the doubling of calcitriol dose [from 28.5 to 50.5 pg/ml (N: 22-111)].

### Complementary analysis

**Biology** revealed inflammatory syndrome. **Repeated microbiological samples** remained negative. Digestive disturbances were investigated by the following tests: **measure of steatocrit and fecal calprotectin, triolein breath test, gastroscopy, ileocolonoscopy, abdominal magnetic resonance imaging** and **enteroclysis**.
Results were compatible with the presence of a steatorrhea with a steatocrit value of 82% although triolein breath test was normal. Fecal calprotectin was 54 µg per g of stool. Duodenal biopsies showed non-specific mild duodenitis and ileal and colonic mucosa were normal. Abdominal imaging were also normal.

### Evolution

**Malabsorption syndrome** secondary to exocrine pancreatic insufficiency was strongly suspected. Indeed, malabsorption and other gastrointestinal disorders occur in about 25 percent of patients [1]. A treatment with **Creon Forte**® was initiated and permitted a resolution of the digestive symptoms (steatorrhea and abdominal pain). The inflammatory syndrome had also resolved under treatment for exocrine pancreatic insufficiency. On the other hand, within a month following the initiation of the treatment with Creon®, the patient developed a **severe hypercalcemia** (corrected serum calcium 3.29 mmol/L) despite the reduction of the oral dose of calcium (2 g/day) and calcitriol (1.5 µg/day). Calcitriol and oral calcium intake was then interrupted until normalization of serum calcium. Thereafter, oral calcium supplements and calcitriol were reintroduced at initial regimen (1.5 g/day and 0.75 µg/day respectively) that maintained the serum calcium between 2.14 and 2.33 mmol/L.

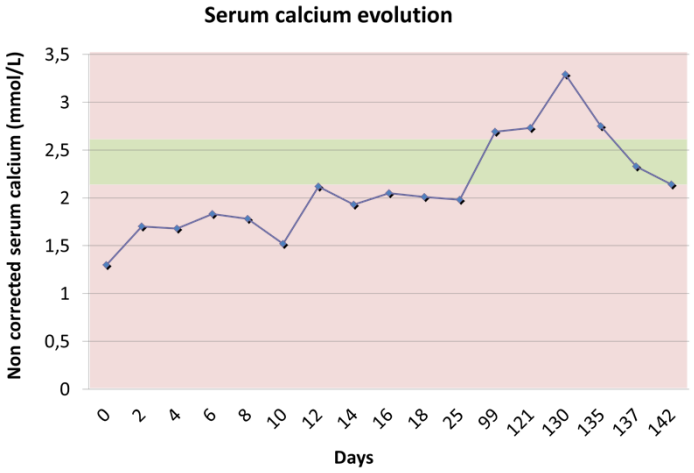


**Figure 1**: Serum calcium evolution *(normal values: 2.12-2.62 mmol/L)*. Severe hypocalcemia was observed at admission (day 0). During hospitalization, intravenous administration of calcium gluconate combined to increased oral doses of calcium and calcitriol allowed a slow normalization of calcemia (day 0 to 25). The addition of Creon Forte® favored the hypercalcemia (day 130) requiring a reduction of oral calcium and calcitriol.

## Conclusion

**High dose of calcium** and **calcitriol use** is limited by the risk of hypercalcemia and by side effects as nephrolithiasis. This case illustrates the **necessity to test new therapies** like subcutaneous recombinant PTH that could be a good alternative for patients with hypoparathyroidism associated with malabsorption.

### Reference

1. J Clin Endocrinol Metab. 1998; 83 (4): 1049

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