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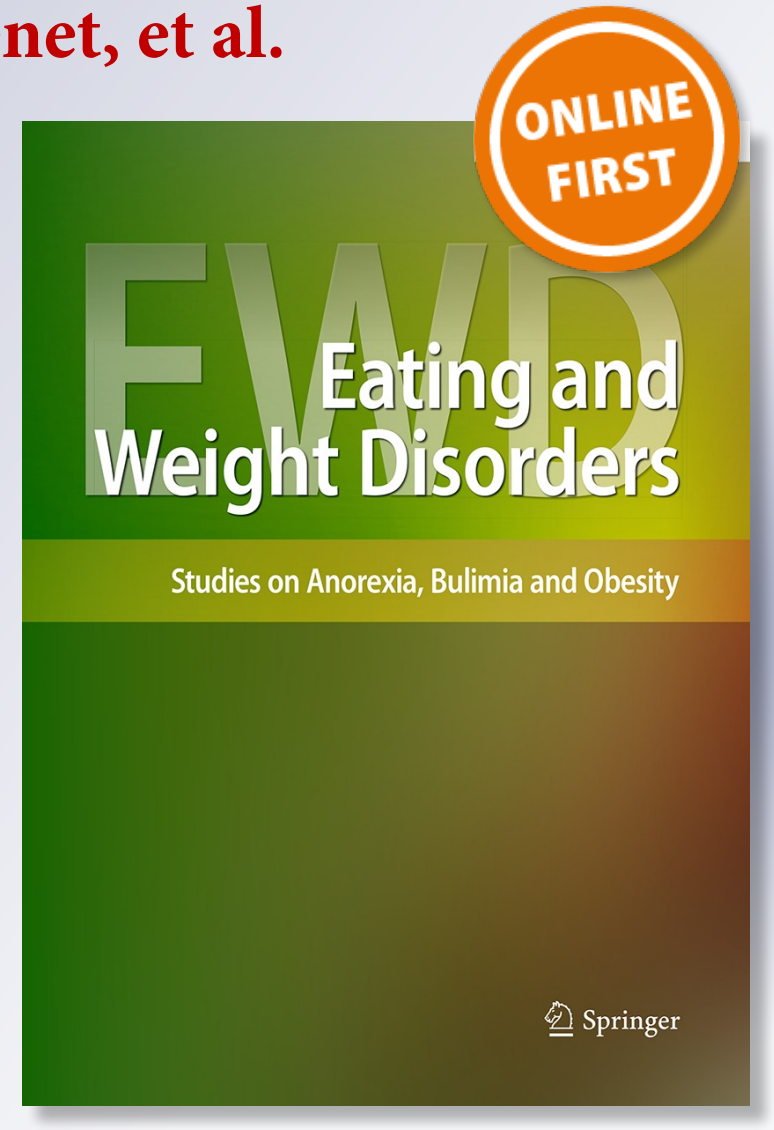

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CASE REPORT

Anorexia nervosa hyperactivity-induced ischemic colitis (ANHIC): a new cause of anaemia

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Abbreviations

MCV	Mean corpuscular volume
MCH	Mean corpuscular haemoglobin
MCHC	Mean corpuscular haemoglobin concentration

Introduction

Anorexia nervosa (AN) is a complex and multifactorial psychiatric pathology with frequent acute or chronic somatic repercussions. It is classically considered that not only malnutrition, metabolic variations and numerous deficiencies in the restrictive sub-type of AN but also digestive lesions associated with other eating disorders sub-type (binge/purging AN, bulimia nervosa, rumination disorder, PICA) can lead to haematological changes [1]. In the literature, anaemia is more specifically and frequently described in AN and mainly as a result of medullary hypometabolism [2]. Despite common representations, cases of anaemia described in restrictive-type AN are not rare and are mostly transient and moderately severe [3]. In contrast, the detection of some atypical biological stigmata such as a severe microcytic anaemia should raise the question of a differential diagnosis, or at least the co-occurrence of an organic pathology, such as inflammatory colopathy or coeliac disease [4]. Other cases of severe and profound anaemia, often developing very suddenly, can be observed in situations of extreme malnutrition with very low body weights and/or very rapid weight loss. The mechanism implicated is gelatinous degeneration of the bone marrow usually affecting the three cell lines, with a risk of multi-organ failure that is life threatening in the short term [5]. Finally, cases of severe anaemia have been described in Lasthénie de Ferjol syndrome, where the eating disorder is associated with severe psychiatric comorbidity [6]. We report the case of a female adolescent patient with AN presenting severe, recurrent episodes of red blood cell depletion, which did not fit the previously described situations, and could be related to a new and underdiagnosed clinical entity we called anorexia nervosa hyperactivity-induced ischemic colitis (ANHIC).

Case presentation

In July 2011, a 17-year-old girl was admitted in our adolescents medical special unit following referral for anorexia nervosa associated with recurrent episodes of acute anaemia for 5 months. Anorexia nervosa (restrictive type) began 3 years before with profound weight loss leading at this time to a first hospitalisation in a paediatric unit. After discharge and a period of drifting without close follow-up, the patient was hospitalised a second time in emergency in the same department with severe weight loss (BMI: 13.6). During 8 months, despite appropriate paediatric cares, her

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medical condition worsened with refusal of enteral feeding, episodes of potomania, various manipulations with marked physical hyperactivity leading to weight loss. At this time, she revealed an intra-familial sexual abuse a few years before. In February 2011, whereas, until this time, red blood cells tests were absolutely normal, a very marked pallor revealed a profound normochromic [MCH 29.1 pg (normal range 27–32), MCHC 33.8 g/dl (normal range 32–36)], normocytic [MCV 86 fl (normal range 80–100)] anaemia [haemoglobin 4.3 g/dl (normal range 12–17)], non-regenerative [reticulocytes 34 g/l (normal range 50–100)] with a profound iron depletion (ferritin 2 ng/ml). In the following weeks, a sudden drop in haemoglobin was observed on two occasions requiring transfusions and intravenous iron perfusion. Because of the deterioration of patient's state and care refusal, the patient was transferred to an adult medical unit specialised in intensive refeeding where she stayed 2 months. The iterative occurrences of red blood cell depletion with severe decrease of haemoglobin levels (normal range 4.3–7.5 g/dl) required 6 transfusions amounting to 15 PRBC infusions (Fig. 1). Melaena was noted on several occasions but two digestive endoscopies realised, respectively, 2–4 days after anaemia episodes and one video capsule endoscopy revealed no macroscopic anomaly. Clinical examination confirmed no other bleeding source (cutaneous, genital, stomatological, proctological, etc.). Biological tests showed no signs of haemolysis, no argument for an inflammatory disease of the digestive track, and myelogram was within normal limits. During this period, massive anxiety and episodes of flashback associated with the post-traumatic syndrome

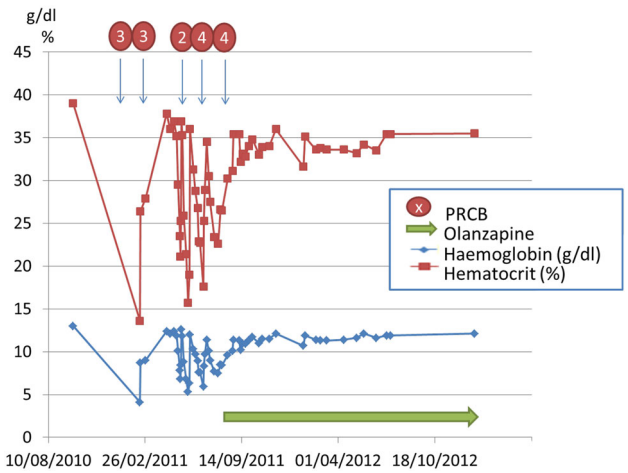

Fig. 1 Evolution of haemoglobin and hematocrit assays from August 2010 to October 2012. Recurrent episodes of severe anaemia with low haemoglobin (Hb 4.3–7.5 g/dl) and hematocrit (HC 13.6–22.6 %) from February to September 2011 required many transfusions amounting to 16 platelets and red blood cells (PRBC) infusions. Normalisation of haemoglobin after PRBC infusions was observed between the episodes of anaemia and definitive normalisation was obtained from September 2011

(post-abuse) were observed leading to an exceptionally intense physical hyperactivity. Because of the weight stagnation, the recurrent and unexplained anaemia episodes, and the intensive psychiatric symptoms the patient was referred to the inpatient unit of the Maison des Adolescents for a multidisciplinary approach.

At admission the BMI was 13.5, with pallor and a cachectic appearance. On day 1, black stools were noted, and melaena was confirmed by the presence of faecal haemoglobin. Confirmation of normocytic [MCV 93 fl (range 80–100)], normochromic [MCH 31.8 pg (range 27–32)], [MCHC 34.1 g/dl (range 32–36)], and massive iron deficiency non-regenerative anaemia with haemoglobin level at 7.7 g/dl (range 12.0–17.0) was noted. Intravenous iron supplementation was administered for a few days. To react to her history of massive physical hyperactivity and her general state of physical and mental exhaustion, major protection measures were instated with agreement of the patient. Continuous and exclusive enteral refeeding, no access to her room during daytime and close overseeing by multidisciplinary team seemed to relieve the patient. Jointly, daily psychiatric interviews and neuroleptic treatment by Olanzapine Velotab Orodispersible, 10 mg/day, were proposed to promote compliance because the patient admitted the habit to spit the tablets in previous hospitalisations (Fig 1).

The patient was able to reduce progressively her physical hyperactivity described by herself as "dance jumping" and "state of trance" in her room, 6 h per day! These revelations were consistent with serious injuries of the feet such as severe hyperkeratosis and heel horn erosions, painful and purulent blisters aggravated by self-mutilation and marked muscular hypertrophy of legs, abdomen and lower limbs (Fig. 2). With progressive refeeding, physical hyperactivity resolution and psychiatric treatment, we observed a regular weight gain (700 g/week) and a progressive normalisation of haemoglobin (+0.5 g/l/week). At discharge in June 2012, haemoglobin was normal (12.1 g/dl) at BMI 16.5 (Fig. 1). Three years after discharge, the patient has a favourable somatic and psychiatric outcome with a BMI 21.4, normalisation of eating behaviours, and no psycho-social troubles requiring special treatment, the anaemia episodes have never relapsed and the last haemoglobin test in 2015 was normal (13.1 g/dl).

Discussion

Anaemia concerns ~21–39 % of patients with anorexia nervosa and is mostly moderate, transitory and asymptomatic. A recent overview article shows that aetiology of anaemia in patients with anorexia nervosa can be in one of these five categories: bone marrow malfunction, deprivation anaemia, haemolysis, loss of haemoglobin, or

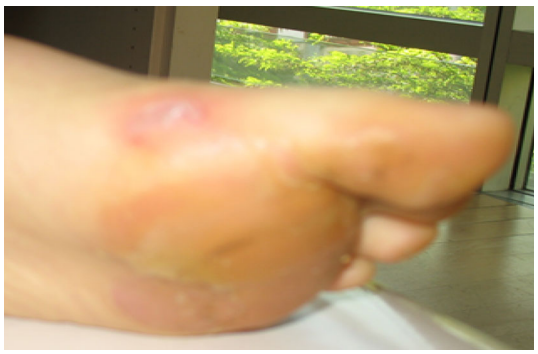

Fig. 2 Serious injuries of the feet resulting from an extremely serious physical hyperactivity. Severe hyperkeratosis and heel horn erosions, painful and purulent blisters aggravated by self-mutilation

inflammation. Nevertheless, cases of anaemia in this context are frequently normochromic, normocytic and multifactorial, and central bone marrow malfunction associated with chronic hypometabolism remains one of the main mechanisms [7]. Usually, anaemia would correct by itself with anorexia proper care including in particular appropriate and progressive refeeding. A continuum is observed from "hypo-functioning" alongside chronic hypometabolism to the gelatinous bone marrow transformation whose frequency is widely underestimated. The severity of the bone marrow degeneration is correlated with the amount and rapidity of weight loss and prognosis can be severe when occurring in a context of multi-visceral failure [8]. Our case concerned acute and recurrent anaemia episodes resulting from deglobulisation associated with a profound iron deficiency in a stable medical condition with careful and appropriate renutrition. However, iron depletion anaemia is fairly infrequent in the first years of anorexia nervosa, on account of the protective effect of amenorrhea and the general restriction in fat and sugar intake, while animal protein, a source of iron, is often still part of the diet [9, 10]. Haemolysis in anorexia nervosa may result either of inappropriate refeeding syndrome or as a result of physical hyperactivity with repeated micro-trauma under soles of feet. But there was no clinical context of inappropriate refeeding syndrome and no haemolysis sign was found on blood tests in our patient. Exceptional cases of factitious anaemia with intentional bloodletting, known as "Lasthénie de Ferjol" syndrome, have been described in severe psychiatric contexts and most of the time concerned binge/purging type of anorexia nervosa [6]. No source of self-inflicted bleeding was found and the psychiatric and global evolution on the long term associated with a complete and persistent haemoglobin normalisation is not in favour of this diagnosis. Because of the repeated melaena episodes, we searched for a digestive cause and due to our patient's massive and "toxicomaniac" physical hyperactivity, we made the link with the non-exceptional cases of anaemia described in intensive running activities where iron deficiency is frequent (3 %) [11]. Physical or sportive hyperactivity, also called "problematic exercise", is a frequent and complex comorbidity, sometimes life threatening, affecting more than 50 % of patients with AN [12]. During intensive and prolonged physical activity there is a blood flow shunt from the splanchnic system towards the muscular system resulting in a massive reduction of the mesenteric flow. Cases of ischemic colitis with occult bleeding in endurance runners are well documented. "Marathon-running-induced ischemic colitis" essentially affects the cecum and ascending colon and are non-gangrenous forms resolving spontaneously [13]. Melaena is compatible with ischemia of this intestinal portion especially because malnutrition frequently decreases intestinal motility increasing blood stagnation in the digestive tract. Endurance runners usually experience gastro-intestinal complaints after exercise. Surprisingly, our anorexic patient did not refer abdominal pain during the recurrent anaemia episodes, but it is known that the perception of the pain is altered in these patients. In most cases, superficial lesions of the intestinal colitis mucosa are observed and can disappear very quickly. So diagnosis requires very early digestive endoscopy, that is to say before the first 48 h, but results are often negative or non-specific as in our case report [14]. Thus, the anaemia aetiology in our anorectic patient is very likely to be due to chronic digestive blood loss caused by an exceptional and compulsive physical hyperactivity as already described in the marathon runner. Chronic malnutrition, hypovolemia, microvascular and coagulation changes are probably self-aggravating factors promoting hypoxia of the colic mucosa in this context. We propose a new and probably underdiagnosed entity, the "anorexia nervosa hyperactivity-induced ischemic colitis" (ANHIC), which could be an unknown anaemia aetiology and a real diagnostic and therapeutic challenge for the multidisciplinary teams dealing with severe hyperactive anorexic patients.

Compliance with ethical standards

Funding No fund was received for this study.

Conflict of interest The author declares that there is no conflict of interest.

Research involving human participants and/or animals *Statement of human rights and ethical approval* All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This article does not contain any studies with human participants performed by any of the authors.

Informed consent Informed consent was obtained from all individual participants included in the study.

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