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Microcytic Anemia Revealing Acromegaly

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Abstract **Case Report**

Acromegaly is a rare endocrinopathy, related to the hyperfunction of the somatotropic axis. We report through this observation an unusual mode of discovery of acromegaly: microcytic anemia. 38-year-old patient, followed for 1 year for microcytic anemia under iron treatment. On clinical examination, the patient presents an anemic syndrome with a frank dysmorphic syndrome evoking acromegaly. The assessment showed a microcytic anemia at 3.8 g/dl for which he received a transfusion of 09 red blood cells. An IGF1 assay and a hypothalamic-pituitary MRI confirmed the diagnosis of acromegaly secondary to a pituitary macro-adenoma measuring 30x25x18mm. Pituitary Function Testing revealed hypogonadotropic hypogonadism, hyperprolactinemia 5 times normal and thyrotropic deficit. The etiological assessment of the anemia revealed several hemorrhagic gastrointestinal angiodysplasia lesions, probably related to his acromegaly. Acromegaly is a classic cause of colonic polyps, but angiodysplasia lesions have not been described in the literature to our knowledge: is it a digestive tropism of acromegaly that continues to grow? Acromegaly is rarely revealed by anemia, the causal link remains to be established.

Keywords: Acromegaly- IGF1-Anemia- Hemorrhagic gastrointestinal angiodysplasia.

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INTRODUCTION

Acromegaly and gigantism are rare disorders caused by growth hormone (GH) hypersecretion with secondary elevation of serum insulin-like growth factor-I (IGF-I) levels, and characterized by progressive somatic disfigurement, and local and systemic clinical manifestations that are associated with increased morbidity and mortality [1, 2]. We report through this observation an unusual mode of discovery of acromegaly: microcytic anemia and a very rare association between acromegaly and gastrointestinal angiodysplasia. Thus, we are wondering about the strength of this association.

OBSERVATION

38-year-old patient, followed for 1 year for microcytic anemia under iron treatment, who has had epigastric pain for 1 month without melena or rectal bleeding with an endocranial tumor syndrome. On clinical examination, the patient presents an anemic syndrome with a typical clinical features evoking acromegaly (figure 1). The biological assessment showed a microcytic anemia at 3.8 g/dl for which he received a transfusion of 09 red blood cells. Acromegaly was confirmed by a very high blood level of IGF1: 1119ng/ml (Normal: 99-229), an absence of GH suppression during the 75 g oral glucose tolerance test (OGTT test), the complement by hypothalamic-pituitary MRI showed the presence of a 30x25x18mm pituitary adenoma (figure 2). Pituitary Function Testing revealed hypogonadotropic hypogonadism, hyperprolactinemia 5 times normal and thyrotropic deficit. As for anemia, his etiological investigation had shown erosive antritis on Esophagogastroduodenoscopy (EGD) with the presence of low-grade Barrett's esophagus dysplasia on the anatomo-pathological study of gastric biopsy, absence of colon polyps on colonoscopy, computed tomography (CT) Enterography was normal. Unlike the hemorrhagic gastrointestinal angiodysplasia lesions described in the video capsule, probably in connection with his acromegaly. The patient underwent transsphenoidal surgical (TSS) resection in July 2022; the Anatomopathological examination reveals a pituitary adenoma without signs of malignancy. Immunohistochemistry detected many adenoma cells positive for GH and prolactin but negative for the other adenohypophysial hormones. Endocrinological reevaluation 3 months after surgery demonstrated biochemical cure: IGF1 level is 167.9ng/ml (normal: 72-

225ng/mL) and post-glucose GH nadir of <1 microgram/liter. The evolution was marked by the disappearance of anemia after 8 months after pituitary surgery with hemoglobin at 13,6 g/dl.

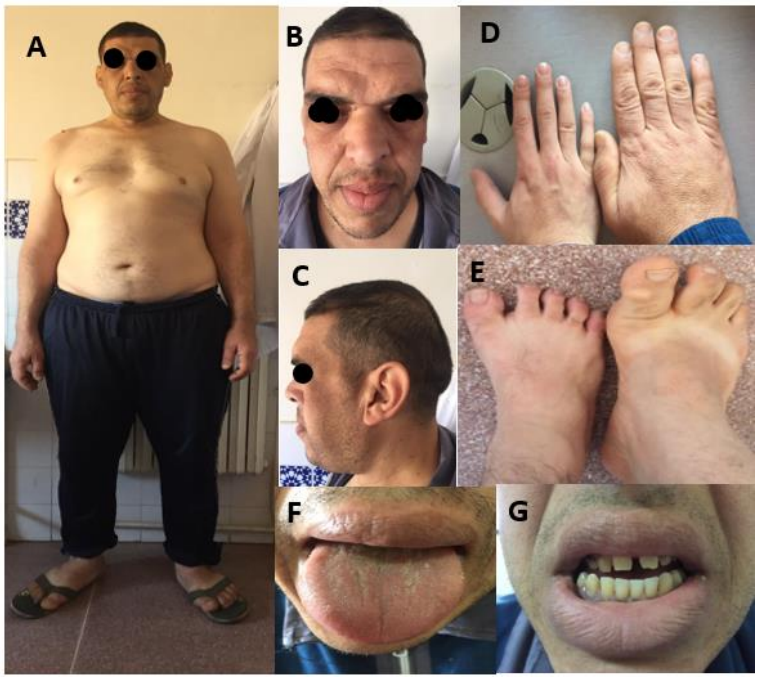

Figure 1: Clinical features of our patient (A: The increased height -B, C: The coarsened facial features with a prognathism; D: Enlarged hand and foot (E) -F: Macroglossia -G: Teeth separation and jaw malocclusion)

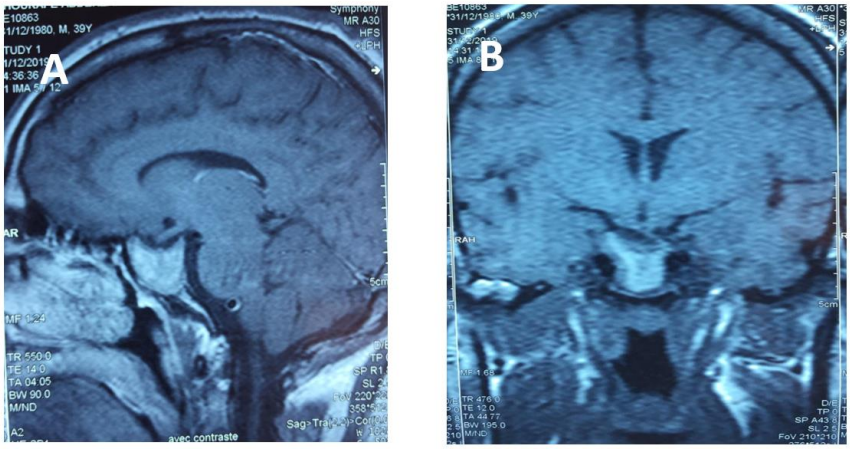

Figure 2: MRI images of pituitary macroadenoma (Sagittal image, (B) Coronal image)

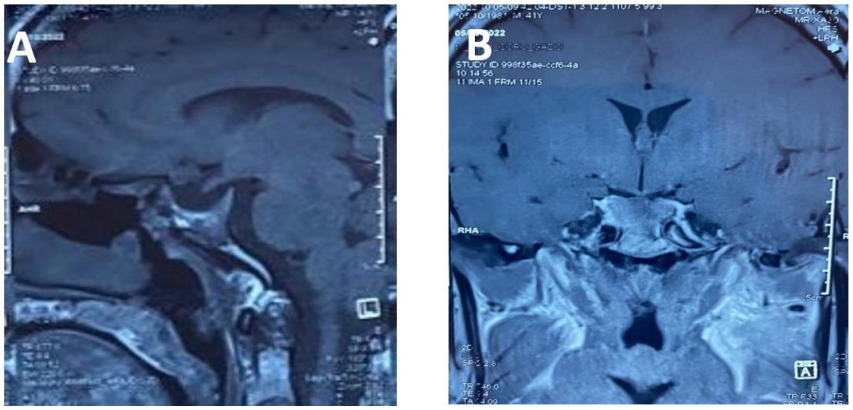

Figure 2: MRI images 3 month after pituitary surgery (A) Sagittal image, (B) Coronal image

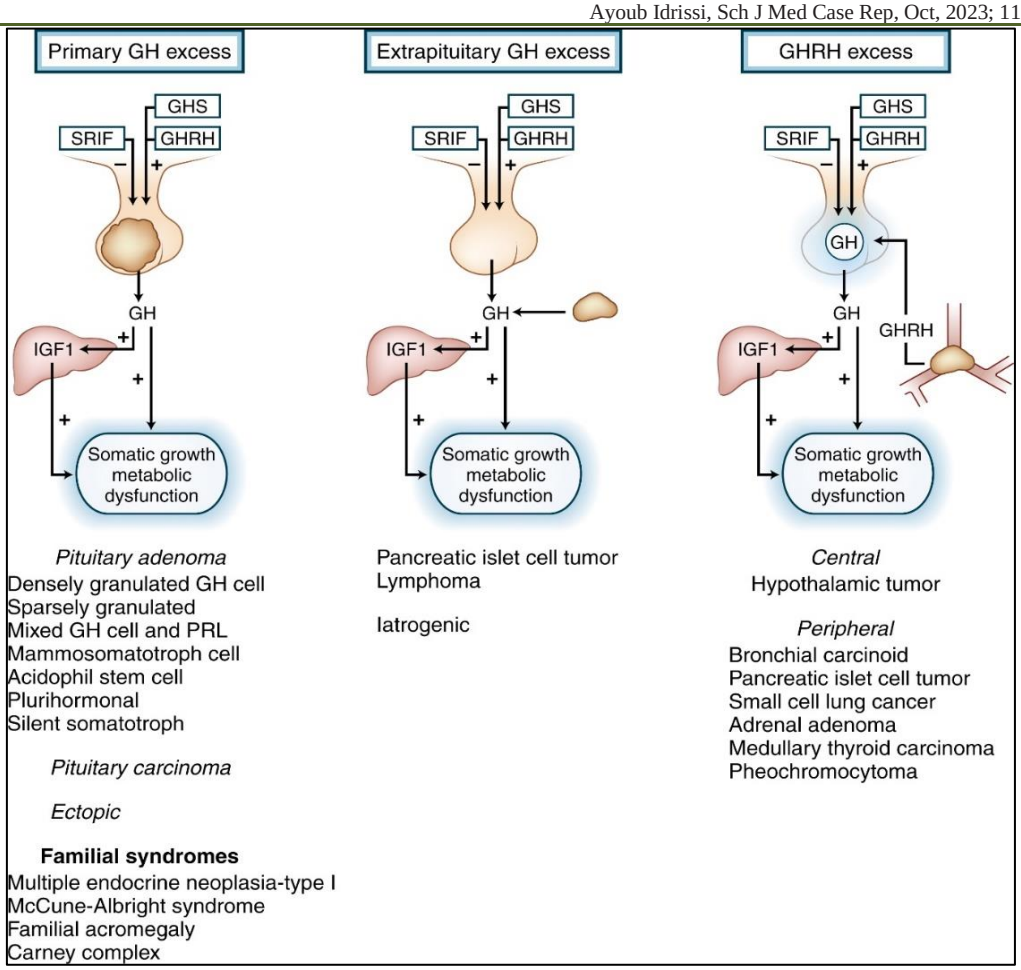

Figure 3: Pathogenesis of acromegaly from [5] **(GH: growth hormone; GHRH: growth hormone–releasing hormone; GHS: growth hormone secretagogue; IGF1: insulin-like growth factor type 1; PRL:prolactin; SRIF: somatostatin (somatotropin release–inhibiting factor)**

DISCUSSION

Acromegaly is a rare chronic disease caused by excessive secretion of GH and consequently of IGF-I. The excess of GH induces insulin-like growth factor-binding protein 3 (IGFBP-3) and IGF-I levels and promotes dysregulated cell growth balance. The symptoms usually appear insidiously, with changes that often go unnoticed. Therefore, more than 10 years can pass from the beginning of the disease until diagnosis. In recent years, it has become recognized that acromegaly is associated with an increased risk of cancer, both in general and with thyroid and colorectal cancer in particular. Moreover, circulating IGF-1 levels within the upper normal range have been associated with elevated risk of breast, prostate, colorectal, thyroid and lung cancers in the general population [3]. The prevalence of acromegaly is estimated to range from 28 to 137 cases per million. Recent surveys indicate an increase in the annual incidence to about 10 cases per million [4].

GH and IGF1 act both independently and dependently to induce features of Hypersomatotropism. Acromegaly is caused by pituitary tumors secreting GH or very rarely by extra pituitary disorders (figure 3). Regardless of the cause, the disease is characterized by elevated levels of GH and IGF1 with resultant signs and symptoms of Hypersomatotropism [5]. A relationship between excess GH and cancer was first suspected five decades ago from studies in hypophysectomized rats when supra-physiological doses of GH administered induced neoplastic changes.

By the mid-1980s, reports appeared suggesting that acromegalic patients may also have an increased risk of mortality from malignancy, notably colorectal cancer. There are various potential biological mechanisms which may explain the association of increased risk of CRC in acromegaly. These include direct GH actions; direct IGF-I actions; hyperinsulinemia; altered IGFBP-3; increased IGF-II and IGFBP-2 levels; altered bile acid secretions; altered local immune response; increased large bowel length; and shared genetic susceptibility [6]. In a meta-analysis, the risks of adenomatous and hyperplastic polyps and colorectal cancer were increased 2.5-fold, 3.6-fold, and 4.4-fold, respectively [7]. The prevalence of polyps was 32% in 165 patients in a case control study, with an estimated relative risk of 6.21 (95% CI, 4.08–9.48). Higher IGF1 levels at diagnosis were more likely associated with distal colon lesions [8]. Hypertrophic mucosal folds and colonic hypertrophy as

well as diverticula are commonly present, and dolicomegacolon may be visualized by CT colonography. Increased incidence of gallbladder polyps and benign prostate hypertrophy have been reported. Although the German Acromegaly Registry does not report higher cancer incidence, a survey of 1512 patients in Italy revealed a moderately increased cancer incidence. Similarly, a nationwide study in Denmark of 529 acromegaly patients revealed an overall cancer SIR of 1.5 (95% CI, 1.2–1.8). Incidence of colorectal, kidney, and thyroid cancers appear to be the most significantly elevated [9, 10]. Thus, although disordered cell proliferation and increased risk for growth promotion of coexisting neoplasms as well as mortality could be anticipated from elevated GH and IGF1 levels, a significantly enhanced cancer incidence has not been consistently observed. Colon cancer appears to be of particular concern, and screening colonoscopy should be performed at diagnosis in all patients.

CONCLUSION

Through our case, we describe an acromegaly with a very high initial blood level of IGF1 at 4.8 times the upper limit of normal, the colonoscopy was normal, in particular there were no colonic polyps unlike the video capsule which objectified a gastrointestinal angiodysplasia, these lesions have not been described in the literature to our knowledge: is it a coincidence or is it a digestive tropism of acromegaly that continues to grow? Acromegaly is rarely revealed by anemia, the causal link remains to be established.

Consent

Written informed consent was obtained from the patient to publish this case report and any accompanying images. No institutional approval was required to publish the case report.

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