

Case Report

Acquired Hypertrichosis Lanuginosa: Typical Presentation and Unusual Association

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Abstract

Paraneoplastic syndrome might be the first clinical manifestation of malignancy. We present a menopausal female with the acquired hypertrichosis lanuginosa (AHL) as an initial clinical presentation of rectal adenocarcinoma, unusually associated with paraneoplastic cerebellar degeneration (PCD) and disseminated intravascular coagulation (DIC).

Keywords: Acquired hypertrichosis lanuginosa, cerebellar degeneration, disseminated intravascular coagulation, rectal adenocarcinoma

Cite this article as: Tančić-Gajić M, Vujović S, Dujmović I, Basta I, Ivović M, Marina LV, Djordjević PB, Micić D. Acquired hypertrichosis lanuginosa: Typical presentation and unusual association. *Arch Iran Med.* 2015; 18(7): 450 – 452.

Introduction

Acquired hypertrichosis lanuginosa (AHL) is a rare paraneoplastic condition characterized by the development of long, thin and unpigmented lanugo hairs that initially cover the face within eyebrows, forehead, ears and nose, but may spread caudally to affect any hair-bearing area, except palmoplantar, genital, and suprapubic regions.¹ Reviewing the English literature, 69 cases of paraneoplastic AHL have been reported in the literature to date.¹⁻⁶ AHL is commonly associated with symptoms of taste or smell disturbance, acanthosis nigricans, hypertrophy of tongue papillae, and glossitis.^{1,6}

An association of the AHL with neurological paraneoplastic manifestations and disseminated intravascular coagulation (DIC) has not been described so far.¹⁻⁶ Here, we report a patient with rectal adenocarcinoma and AHL as an initial clinical feature, followed by anti-Yo positive paraneoplastic cerebellar degeneration (PCD) and DIC.

Case Report

A 60-year old woman was admitted to the Clinic of Endocrinology due to a 6-month history of hypertrichosis along with a 2-month history of decreased appetite, weight loss, diarrhea and occasional bloody stools. In the next period, she complained of subacute development of speech difficulties and unsteady gait. She was presented to a gastroenterologist prior to hospital admission, however she refused rectosigmoidoscopy. Past medical history revealed the onset of menopause at the age of 53. No previous topical or systemic drug treatments had been administered. Family history was unremarkable. Physical examination revealed cachexia, while the whole face, especially forehead, ears and nose

as well as neck, thorax and back were covered with numerous, widespread, fine, long, non-pigmented hairs (Figure 1). Neither signs of pulmonary congestion nor any other symptoms of overt heart failure were found. Digital rectal examination confirmed the presence of blood in the rectum. The rest of her physical examination was normal. Neurological examination revealed the presence of mild to moderate dysarthria, bilateral horizontal nystagmus, limb ataxia and ataxic gait. Electrocardiogram was normal. On admission, routine blood and urine tests were normal except mild thrombocytopenia ($107 \times 10^3/\mu\text{l}$). Hemocult test in the stool was positive. Androgen and cortisol levels were normal. Serum carcinoembryonic antigen, carbohydrate antigen 19 – 9 and cancer antigen 15 – 3 levels were elevated: 70.8ng/mL, 1928.0 U/mL and 220.4U/mL, respectively (normal levels: < 2.5ng/mL, < 40U/mL and < 30U/mL, respectively).

On the fifth day of hospitalization the patient became somnolent, disoriented, with left hemiplegia. Brain MRI performed on the sixth day of hospitalization revealed the presence of multifocal bilateral non-enhancing, predominantly cortical ischemic infarctions (Figure 2 A, B), and the presence of a mild cerebellar atrophy (Figure 2C). Antinuclear and anticardiolipin antibodies were negative and lupus anticoagulant was normal. Cerebrospinal fluid (CSF) was acellular with normal levels of CSF protein and CSF/serum glucose, and had normal CSF bacteriology and mycology cultures. CSF immunoglobulin G oligoclonal bands were negative. Echocardiogram did not show intracavitary masses. Color Doppler ultrasound of the carotid and vertebral arteries was unremarkable. Osmotherapy with mannitol and parenteral anticoagulation resulted in slight improvement. The patient becomes oriented, but was still hemiplegic. Testing for onconeural (anti-Hu, Yo, Ri, CV2, Ma2, GAD and amphiphysin) antibodies by indirect immunofluorescence revealed positive anti-Yo antibodies (titer 1:100) (Euroimmune, Lubeck, Germany) (Figure 3). Repeated hemostasis parameters showed the following pattern: serum fibrinogen levels gradually decreased from 4.2 to 1.2g/L; thrombocyte count decreased from 111 to $67 \times 10^3/\mu\text{L}$, while we observed an increase in: partial thromboplastin time from 33.2 to 44.3s, prothrombin time from 11.0 to 14.7 second (normal range: 0.97 – 1.32 second) and D dimer from 4.5 to 11.2mg/L. Such a pattern

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Figure 1. Lanugo type hair on the patient's face and neck in acquired hypertrichosis lanuginosa.

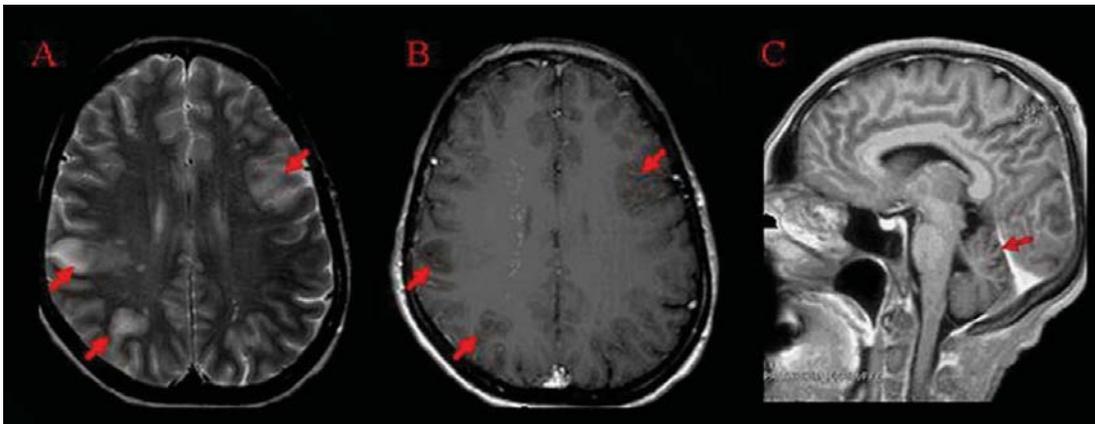


Figure 2. Brain magnetic resonance imaging scans showing: **A**) multiple T2-weighted hyperintense lesions (arrows) with no contrast enhancement; **B**) suggestive of cerebral infarctions and **C**) mild cerebellar atrophy in a patient with paraneoplastic chronic disseminated intravascular coagulation associated with anti-Yo positive cerebellar degeneration.

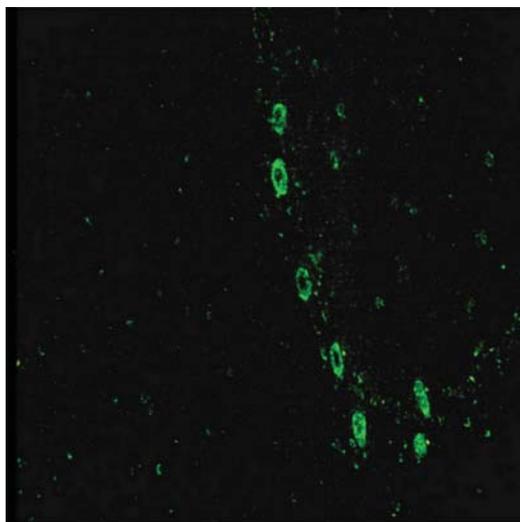


Figure 3. Indirect immunofluorescence: positive serum anti-Yo antibodies in patient with rectal carcinoma (titer, 1:100).

indicated the presence of chronic DIC.⁷ A screening protocol for malignancy was performed and colonoscopy revealed a mass located at the eighth centimeter from the anal verge, histologically diagnosed as a well-differentiated rectal adenocarcinoma. Multislice computerized tomography of the abdomen showed a 56 mm × 33 mm × 45 mm rectal tumor with multiple enlarged para-aortic, on the left and right iliac lymph nodes. No mediastinal, hepatic or other distant metastatic diseases were demonstrated.

Unfortunately, the patient did not accept any kind of cancer treatment in the regional oncology hospital and was further allocated to a palliative care program until her death.

Discussion

The first report of paraneoplastic AHL dates back to 1865 year when Turner described AHL in a 42-year-old woman with breast cancer.¹ In the patient presented here, clinical finding of excessive lanugo type hair, without a male pattern of body hair and signs of virilization implied on a diagnosis of the AHL. Non-malignant AHL has been linked to metabolic and endocrine diseases or may be induced by some drugs.^{1,3} Our patient did not take any drugs related with hypertrichosis and had no endocrine abnormalities. The largest series of patients with AHL have been published by Slee, et al.¹⁻⁶ In women paraneoplastic AHL is most commonly associated with colorectal carcinoma, as in our case, followed by lung cancer and breast cancer. Tumour-produced growth factors are hypothesised to be responsible for the initiation of hair follicle growth in AHL, although the exact pathogenesis of this condition is unknown.¹ An association of AHL and PCD has not been reported so far. PCD is one of the “classical” paraneoplastic neurological disorders, often leaving patients with significant disability resulting from irreversible Purkinje cell destruction.⁸ PCD is often associated with anti-Yo antibodies that are directed against human cerebellar degeneration-related protein 2 (CDR2), which is normally expressed on Purkinje cells in the cerebellum and aberrantly expressed in some cancers.⁹ The onset of PCD is usually subacute, with rapid development of a severe pancerebellar syndrome in less than 12 weeks.⁸ Brain MRI in PCD rarely show cerebellar swelling and gadolinium enhancement in acute phase, but in the later stages of the disease cerebellar atrophy is often found.^{8,9} Our patient had a mild cerebellar atrophy. Most likely the underlying tumors in patients with PCD are breast or gynecological malignancies,^{8,9} whereas colorectal carcinoma is present in rare cases and has been published only once to date. It was anti-Hu positive PCD.¹⁰ Anti-Yo positive PCD may be associated with gastrointestinal adenocarcinoma (esophageal, gastric, gastroesophageal junction) and has not yet been described in patients with rectal adenocarcinoma.¹¹ To the best of our knowledge, this is the first report of PCD with positive anti-Yo antibodies associated with a rectal adenocarcinoma.

In addition to PCD, our patient suffered from a stroke due to the development of chronic DIC. The relationship between malignancies and DIC has been described in 10–15% of patients with metastatic solid tumours.¹² DIC in malignancy appears in acute and chronic form.⁷ It is believed that the abnormal expression of pro-coagulant tissue factor on tumour cells and/or the vessel surface have pivotal roles in activation of the extrinsic coagulation pathway through a complex binding with factor VII.¹²⁻¹³ DIC in cancer patient usually has a less fulminant clinical presentation leading to vascular thrombosis and ischemia as it was in our case.^{12,13} If

liver function is not compromised, enhanced synthesis of coagulation proteins may mask the ongoing consumption of coagulation factors, and thrombocytopenia may be the most prominent sign of ongoing DIC, as we reported here.¹³ Optimal management of DIC associated with cancer is based on the treatment of the underlying malignancy in combination with supportive anticoagulant therapy.^{12,13} Successful anti-cancer therapy is also associated with regression of the hair growth in AHL, but on the other hand is not usually associated with the improvement of PCD with positive anti-Yo antibodies.^{1,8} Unfortunately, our patient did not accept any suggested cancer treatment protocol.

Our case expands the spectrum of malignancies associated with anti-Yo PCD and indicates the possibility of a combined paraneoplastic syndromes in a single patient. The timely recognition of ALH as a paraneoplastic disorder might lead to the detection of a malignancy at an early and possibly treatable stage.

Acknowledgments

This work was supported by research grants of the Ministry of Education and Science of the Republic of Serbia: project No 175067 (MTG, SV, MI, LVM, DM), project No 175031 (ID) and 175087 (IB). The authors declare no conflicts of interest.

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