

Striae rubrae: Cushing's syndrome

Lecturer Ana VALEA^{1,2}, MD, PhD, Assist. Prof. Florica SANDRU^{3,4}, MD, PhD,
Lecturer Mihai Cristian DUMITRASCU^{3,5}, MD, PhD, Assist. Prof. Simona Elena ALBU^{3,5}, MD, PhD,
Lecturer Mara CARSOTE^{3,6}, MD, PhD

¹ Clinical County Hospital, Cluj-Napoca, Romania

² "Iuliu Hatieganu" University of Medicine and Pharmacy, Cluj-Napoca, Romania

³ "Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania

⁴ Elias Emergency University Hospital, Bucharest, Romania

⁵ Emergency University Hospital, Bucharest, Romania

⁶ "C.I. Parhon" National Institute of Endocrinology, Bucharest, Romania

ABSTRACT

Striae rubrae or red striae are found in different circumstances like pregnancy, weight gain and Cushing's syndrome regardless of endogenous or exogenous type. This type of skin lesion is commonly found in general population and usually does not underline a severe condition. The histological aspect that involves the stretch marks is the destruction of the dermal fibbers and their local network. The fibbers have receptors for glucocorticoids. A secondary epidermal anomaly is also seen. In benign scenarios the prevention with topic applications is still a matter of debate while therapy lasers of different types might help. In cases with pathological glucocorticoids excess the removal of the source improves the skin lesions yet not completely, they become white. We aim to introduce two cases of Cushing's disease of different origins to whom impressive red striae were positive from the presentation. Red striae may be the hallmark of Cushing's syndrome in association with different cardio-metabolic and/or bone complications. Despite the remission of the glucocorticoid excess the skin lesions are not completely reversible.

Keywords: striae rubrae, Cushing's syndrome, endocrine tumour

Abbreviations

ACTH = Adrenocorticotrop hormone
CRH = Corticotropin-releasing hormone
DXA = Dual-Energy X-Ray Absorptiometry

INTRODUCTION

Striae rubrae or red striae are found in different circumstances like pregnancy, weight gain and Cushing's syndrome regardless of endogenous or exogenous type (1,2). This type of skin lesion is commonly found in general population and usually does not represent a severe condition (1,2). The histological aspect that underlines the stretch marks is the destruction of the dermal fibbers and their local network (1,2). The fibbers have recep-

tors for glucocorticoids (1,2). A secondary epidermal anomaly is also seen at the skin lesions (1,2). In benign scenarios the prevention with topic applications is still a matter of debate but it might work (3,4). Lasers therapy of different types might be also useful (3,4). In cases with pathological glucocorticoids excess the removal of the source improves the skin lesions yet not completely, they become white but usually the scars of any aspects are permanent.

Corresponding author:

Assist. Prof. Florica Sandru
E-mail: florysandru@yahoo.com

AIM

We aim to introduce two cases of Cushing’s disease to whom impressive red striae were positive from the presentation.

MATERIAL AND METHOD

This is a two cases report. The clinical and investigations profile is also introduced.

CASE REPORT

Case 1

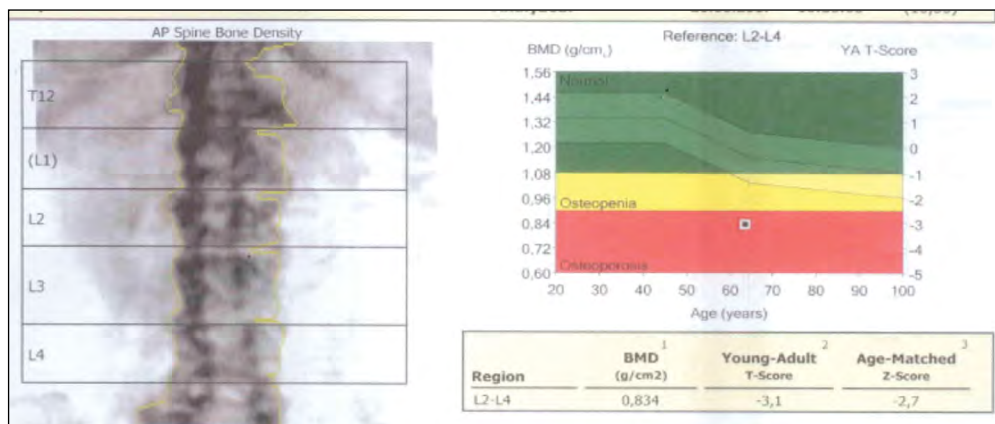
This is a 63 year old female who was a former smoker. She is known with type 2 diabetes mellitus requiring insulin therapy (more than 50 Units per day) from several years. She also associates high blood pressure partially controlled under medication. The family medical history is negative.

She was admitted because she developed red striae and aggravated the glycaemia profile de-

spite insulin therapy. Also she has obesity (a body mass index of 40 kg/sqm) and a newly detected low trauma vertebral fracture at the level of thoracic spine (Figure 1). DXA (Dual-Energy X-Ray Absorptiometry) showed the lowest T-score of -3.3 SD. She had hypovitaminosis D (25-hydroxyvitamin D of 7 ng/ml, with normal levels between 30 and 100 ng/ml), and normal parathormon levels as well as blood bone turnover markers.

She was referred for the suspicion of Cushing’s syndrome. Cushing’s disease was confirmed based on basal morning plasma ACTH (adrenocorticotrop hormone) between 20 and 38 pg/ml in different days (normal levels between 3 and 66 pg/ml) and non-suppressible plasma morning cortisol of 20 µg/dl after 2 days X 2 mg dexamethasone suppression screening test (normal levels of cortisol for the consecutive third day of less than 1.8 µg/dl) and a 60% reduction of plasma baseline cortisol after 2 days X 8 mg dexamethasone suppression pathogenic test (a reduction of more than 50% referring to baseline morning plasma cortisol is sug-

Lumbar spine



Femoral neck

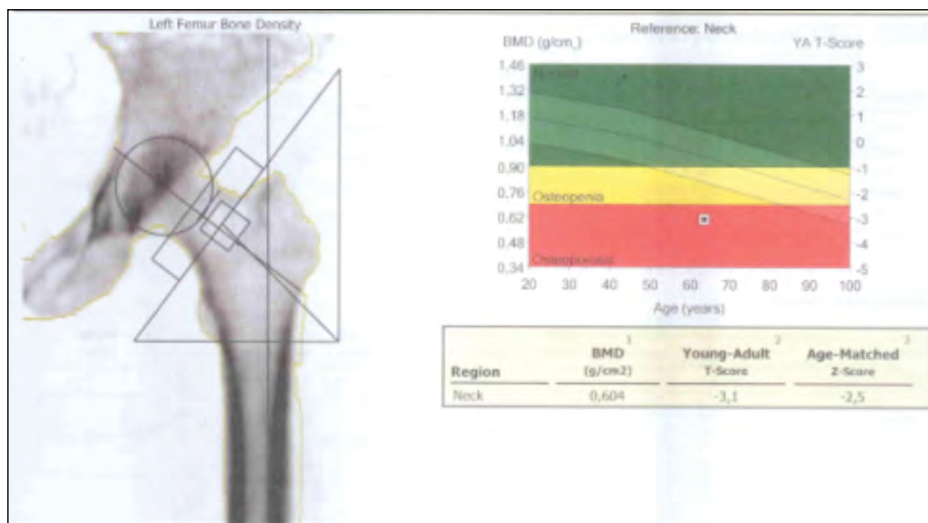


FIGURE 1. DXA report showing osteoporosis based on T-score on an menopausal woman with Cushing’s disease

gestive for a corticotropinoma). Pituitary micro-corticotropinoma was identified at magnetic resonance imagery and then the subject was referred for hypophysectomy which she refused so radiotherapy of gamma knife type was further recommended (Figure 2).



FIGURE 2. Computed tomography of the pituitary region: Micro-corticotropinoma on adult female with cardio-metabolic and bone performances

tion of liver enzymes within 3 weeks. Also, within the next weeks the patient lost weight, normalised glycaemia and blood pressure without any medication while the red striae remained white.

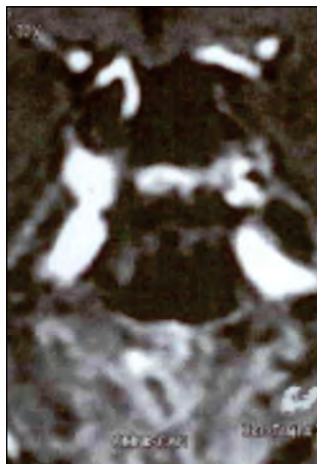


FIGURE 3. Magnetic resonance imagery of pituitary micro-corticotropinoma on a young adult male

Case 2

This is a 33-year old non-smoking male who developed within 6 months multiple red striae at the level of arm, legs, abdomen in addition to 10 kg increase, loss of his physical performances, high blood pressure, and newly detected diabetes mellitus. So he was referred for the suspicion of Cushing's syndrome. The family medical records are negative.

The baseline plasma morning ACTH is high-normal of 51 pg/ml (with normal ranges between 3 and 66 pg/ml), the circadian rhythm of plasma cortisol is inverted. The values of plasma morning cortisol do not suppress after low dose of dexamethasone inhibition test but at 2 days X 8 mg dexamethasone suppression test the level of plasma cortisol decreased to 8 µg/dl (which means > 50% reduction from baseline value suggesting a corticotropinoma). The pituitary tumour has 0.28 cm at magnetic resonance imaging and selective hypophysectomy was done (Figure 3). The post-operative second day plasma cortisol was not detectable and the patient needed hydrocortisone substitution. Yet the subject was not compliant to oral therapy and he was admitted 10 days after neurosurgery was done as an emergency for acute secondary adrenal insufficiency also associating high levels of liver enzymes ALT of 533/ repeated of 424 U/l (normal levels than 55 U/l), AST of 536/ repeated 525 U/l (normal values less than 34 U/l). After adequate intravenous therapy of acute insufficiency, the viral hepatic markers were tested and found negative with a progressive normaliza-

DISCUSSION

Several aspects need to be discussed regarding these cases.

Normal ACTH and corticotropinoma

The first case had mid-normal values of ACTH even the Cushing's disease was confirmed based on cortisol values during dynamic tests. This is not so rare but it represents a challenge of the diagnosis (5,6). Interferences with ACTH assays cause a high variability, and falsely increased or decreased results have been reported (5,6). In addition to mentioned testes, also late-night salivary cortisol or free urinary cortisol are useful as screening tools as well as dexamethasone-CRH (corticotropin-releasing hormone) test for pathogenic tests (7,8).

Limited resources for Cushing's disease

The female case we introduced showed that the patient's option must be taken into account. If surgery of the pituitary tumour is not feasible or successful, pituitary radiotherapy is needed (with a delay of action), especially in adults who are not of reproductive age (9). Pasireotide might be a bridge treatment but the complicated diabetes mellitus requiring high doses of daily insulin relatively limits its use (9). Also in this case surgery of the both adrenal glands may become a solution if the control of the disease is not otherwise achieved (10,11,12).

Tumour-related osteoporosis

The menopausal female case was actually referred for endocrine check-up after she suffered a low-trauma vertebral fracture. Glucocorticoid osteoporosis represents the most frequent cause of secondary osteoporosis; yet in this particular case other components involved in osteoporotic fragility fractures mechanisms are involved: menopause-related estrogens deficiency, obesity and type 2 diabetes mellitus and potentially insulin therapy and hyperlipidemia (13,14). As expected for a patient with metabolic complications, low levels of vitamin D were identified but associating a normal parathormone value (15,16). Also, the blood bone turnover markers were irrelevant even in glucocorticoid-induced bone loss a high resorption with low bone formation is presented, as well as blunted turnover in diabetes mellitus (17,18,19).

Acute adrenal insufficiency after selective hypophysectomy

The young male case introduces a successful event: the presence of adrenal insufficiency after

corticotropinoma removal even the patient was not compliant to oral prednisone therapy and he was admitted as an emergency. The rate of tumour control after neurosurgery for pituitary tumours mainly depends on tumour anatomy as size and sinus cavernous invasion and surgeon's skills (between 30 and 90%) (20,21). The presence of non-detectable levels second day after surgery as well as the post-operative adrenal insufficiency for as long as possible represents the hallmarks of Cushing's disease control (22).

CONCLUSION

Red striae may be the hallmark of Cushing's syndrome in association with different cardio-metabolic and bone complications. Despite the remission of the glucocorticoid excess the skin lesions are not completely reversible.

REFERENCES

- Oakley AM, Patel BC. Stretch Marks (Striae). StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2019-2018 Dec 28.
- Kasielska-Trojan A, Sobczak M, Antoszewski B. Risk factors of striae gravidarum. *Int J Cosmet Sci.* 2015 Apr; 37(2):236-40.
- Wollina U, Goldman A. Management of stretch marks (with a focus on striae rubrae). *J Cutan Aesthet Surg.* 2017 Jul-Sep; 10(3):124-129.
- Hague A, Bayat A. Therapeutic targets in the management of striae distensae: A systematic review. *J Am Acad Dermatol.* 2017 Sep; 77(3):559-568.e18. doi: 10.1016/j.jaad.2017.02.048.
- Pecori Giraldi F, Sacconi A, Cavagnini F; Study Group on the Hypothalamo-Pituitary-Adrenal Axis of the Italian Society of Endocrinology. Assessment of ACTH assay variability: A multicenter study. *Eur J Endocrinol.* 2011 Apr; 164(4):505-12.
- Toprak B, Yalcin H, Ari E, Colak A. EDTA interference in electrochemiluminescence ACTH assay. *Ann Clin Biochem.* 2016 Nov; 53(6):699-701.
- Alwani RA, Schmit Jongbloed LW, de Jong FH, van der Lely AJ, de Herder WW, Feelders RA. Differentiating between Cushing's disease and pseudo-Cushing's syndrome: Comparison of four tests. *Eur J Endocrinol.* 2014 Mar 8; 170(4):477-86.
- Bansal V, El Asmar N, Selman WR, Arafah BM. Pitfalls in the diagnosis and management of Cushing's syndrome. *Neurosurg Focus.* 2015 Feb; 38(2):E4.
- Pivonello R, De Martino MC, De Leo M, Simeoli C, Colao A. Cushing's disease: The burden of illness. *Endocrine.* 2017 Apr; 56(1):10-18.
- Valea A, Ghervan C, Carsote M, Albu SE, Georgescu CE. Different surgical options in Cushing's disease. *Journal of Surgical Sciences.* 2016; 3(1):39-43.
- Paduraru DN, Nica A, Carsote M, Valea A. Adrenalectomy for Cushing's syndrome: Do's and don'ts. *Journal of Medicine and Life.* 2016; 4(9):334-341.
- Carsote M, Ghemigian A, Valea A, Dumitrascu A, Chirita C, Poiana C. Subclinical Cushing's syndrome with bilateral adrenal tumours in a patient with gallbladder multiple stone: Therapeutical options. *Ars Medica Tomitana.* 2015; 3(21):124-127.
- Poiana C, V.Radoi, Carsote M, Bilezekian J. New Clues that May Link Osteoporosis to the Circulating Lipid Profile. *Bone Research* 2013; 1(3):260-266.
- Carsote M, Radu O, Dumitrascu A, Terzea D, Valea A, Ghemigian A. Bone and menopause: Threshold of intervention. *Romanian Medical Journal.* 2016; LXIII(3):233-236.
- Albu SE, Geleriu A, Carsote M, Mihai A, Vasiliu C, Poiana C. The vitamin D status in menopausal women. *Archives of Balkan Medical Union.* 2015. 50(2):275-277.
- Albulescu DM, Carsote M, Ghemigian A, Popescu M, Predescu AM, Tuculina MJ, Bugala AS, Bataiosu M, Marinescu RI, Dascalu IT, Stan M, Cumpata CN, Bechir ES. Circulating 25-hydroxycholecalciferol in relationship to Central Dual-Energy X-Ray Absorptiometry Assesses. A clinical study. *Rev.Chim.* (Bucharest). 2018; 69(12):3683-3687.
- Radu L, Carsote M, Gheorghisan-Galateanu AA, Preda SA, Calborean V, Stanescu R, Gheorman V, Albulescu DM. Blood Parathyrin and Mineral Metabolism Dynamics. A clinical analyze. *Rev.Chim.* (Bucharest). 2018; 69(10):2754-2758.
- Carsote M, Preda SA, Mitroi M, Camen A, Radu L. Serum Osteocalcin, P1NP, Alkaline Phosphatase, and CrossLaps in Humans: The relationship with body mass index. *Rev. Chim.* (Bucharest). 2019; 70(5):1615-1618
- Bechir ES, Carsote M, Tuculina MJ, Bataiosu M, Dascalu IT, Raescu M, Rica R, Daguci C, Daguci L, Predescu A, Andrei OC, Mercut R, Cumpata CN. Biochemical Analysis of Mineral Metabolism and Central Bone Mineral Density in 157 Adult Women. *Rev.Chim.* (Bucharest). 2018; 69(12):3565-3568
- Darwish H, El-Hadi U, Haddad G, Najjar M. Management of Pituitary Adenomas: Mononostri Endoscopic Transsphenoidal Surgery. *Basic Clin Neurosci.* 2018 Mar-Apr; 9(2):121-128.
- Lonser RR, Nieman L, Oldfield EH. Cushing's disease: Pathobiology, diagnosis, and management. *J Neurosurg.* 2017 Feb; 126(2):404-417.
- Tritos NA, Biller BMK. Current management of Cushing's disease. *J Intern Med.* 2019 Nov; 286(5):526-541.