

Pale skin: An adrenal cancer?

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ABSTRACT

Adrenal carcinoma is a complex orphan disease with a very poor prognosis. The evolution is rapid and in cases with suggestive symptoms the diagnosis may be established earlier in order to improve the outcome. One third of the patients are negative for a clear hormonal expression or they have an atypical presentation. We introduce an adult patient diagnosed with adrenal carcinoma and a rapid lethal outcome who initially presented with pale skin and non-specific abdominal pain. A multidisciplinary team is essential for adequate diagnosis and prompt intervention. Severe bleeding at the level of the adrenal carcinoma causing symptomatic anaemia is a rare event. The prognosis in adrenocortical carcinoma is severe and the presence of humoral hypercalcaemia represents a sign of short survival time.

Keywords: pale skin, abdominal tumour, adrenal cancer

Abbreviations

ACTH = adrenocorticotrophic hormone PTH = parathormone
BMD = bone mineral density PTHrP = PTH related protein
DXA = Dual-Energy X-Ray Absorptiometry SD = standard deviation
MEN 2A = multiple endocrine neoplasia

INTRODUCTION

Adrenal carcinoma is a complex orphan disease with a very poor prognosis (1,2). The evolution is rapid and in cases with suggestive symptoms the diagnosis may be established earlier in order to improve the outcome which is still dramatic in most cases (1,2). One third of the patients are negative for a clear hormonal expression or they have an atypical presentation (3,4). The risk of malignancy at the level of an adrenal incidental involving an adrenal carcinoma is 0.1% (5,6). Typically the abdominal pain and mass is associated with Cushing's syndrome but some other compli-

cations are related to anaemia, rapidly developing hirsutim in females, persistent infections of complications of the high blood pressure like stroke and acute myocardial infarct (7,8). After tumour removal the prognosis is improved through Cushing's syndrome control and medical therapy continues with mitotane (9,10,11).

AIM

We introduce an adult patient case diagnosed with adrenal carcinoma and a rapid lethal outcome who initially presented with pale skin and non-specific abdominal pain.

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MATERIAL AND METHOD

This is a case presentation type of report. The endocrine and imaging profile is provided. The investigations required a multidisciplinary team.

CASE REPORT

Presentation

This is a 49-year old male coming from endemic area with irrelevant family and personal medical background. He was admitted in different medical services for developing within weeks pale skin, asthenia and non-specific abdominal pain. After several hospitalisations, the diagnosis was not established yet, so he had an abdominal and thorax computed tomography done without contrast and an adrenal tumour of 10 cm was detected.

Endocrine panel

On admission, the investigations confirmed anaemia with hyposideremia (haemoglobin of 8 g/dl, normal above 14 g/dl) with rapid decreased of the haemoglobin (within days). The endocrine profile showed high serum calcium of 11.7 g/dl (normal between 8.5 and 10.2 mg/dl) with suppressed PTH (parathormone) of 1 pg/ml (normal levels between 15 and 65 pg/ml) with an increase of total serum alkaline phosphatase 1.5 time above normal upper limit and normal level of 25-hydroxyvitamin D of 40 ng/ml (normal: 30-100 ng/ml).

He associates multinodular goitre with small nodules normal thyroid function and negative antibodies against thyroid (Figure 1). The serum calcitonin is two times above the normal upper limit.



FIGURE 1. Thyroid ultrasound shows micronodular goitre on an adult male with adrenocortical cancer and mild increase of calcitonin

The morning plasma cortisol is high of 35 µg/dl (normal less than 21 µg/dl) and there is no sup-

pression after the administration of 2 day X 2 mg dexamethasone during test. ACTH (adrenocorticotrophic hormone) is mid-normal of 35 pg/ml (normal: 3-66 pg/ml) associated with normal serum levels of chromogranin A, plasma metanephrines and normetanephrines.

Other imaging scans were done. Whole body bone scintigram was negative for bone metastases (Figure 2). DXA (Dual-Energy X-Ray Absorptiometry) showed normal BMD (bone mineral density) for age (Figure 3).

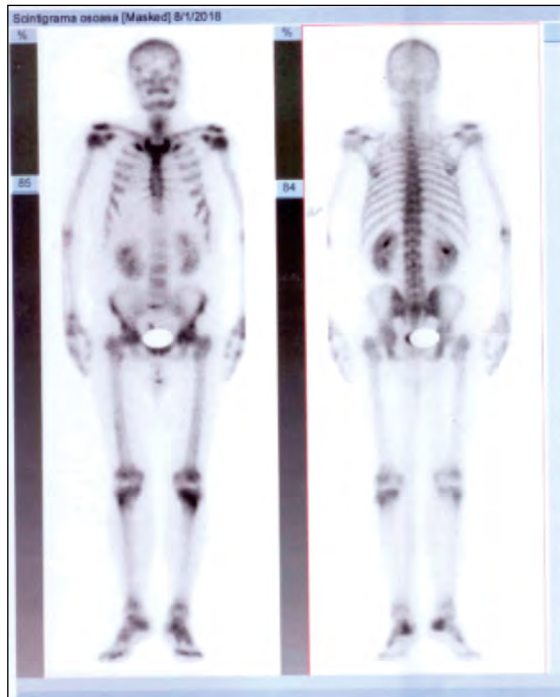


FIGURE 2. Whole body bone scintigram negative for bone metastasis in a patient with high calcium and suppressed PTH associating a malignant right adrenal tumour

Abdominal ultrasound and then computed tomography was re-done and showed a rapid right adrenal tumour increase to 13 cm maximum diameter and liver invasion in addition to intra-tumour necrosis and secondary lung spreading (Figure 4).

Outcome

The patient was transferred for palliative tumour resection but he died within days before the intervention because of massive intra-tumour haemorrhage.

DISCUSSION

Hipercalcitoninemia

The increase of calcitonin in this case may be considered a non-specific neuroendocrine tu-

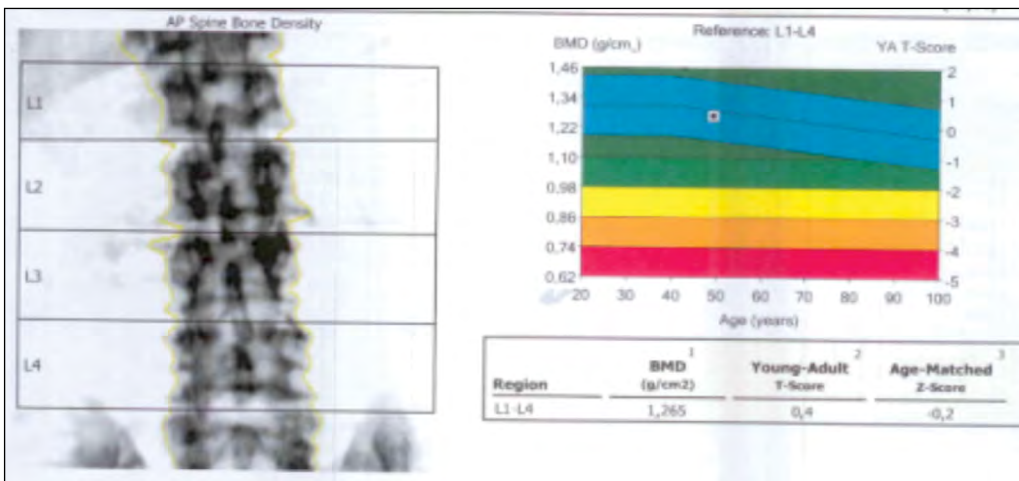


FIGURE 3. Normal central DXA (lumbar spine, GE Lunar Prodigy device)

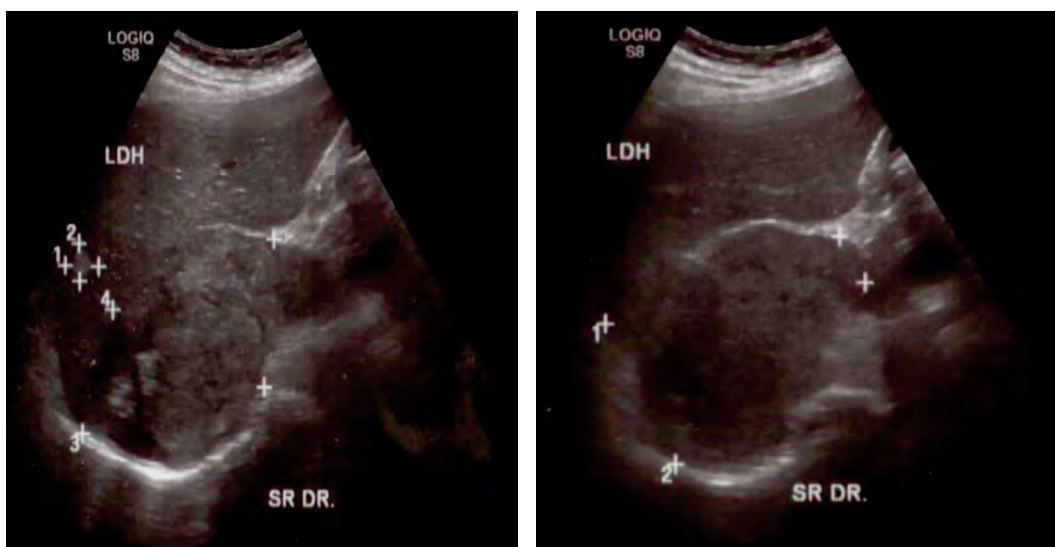


FIGURE 4. Large right adrenal tumour with liver invasion at abdominal ultrasound (different sections)

mour. It is less possible to be associated with a synchronous medullary thyroid cancer since the values of calcitonin were only mildly increased and the thyroid ultrasound pattern was not suggestive. Fine needle aspiration might have been an investigational tool but not a feasible option due to the emergency aspect. MEN 2A (multiple endocrine neoplasia) syndrome also involves at least one adrenal tumour and increased calcitonin but this was not such a case (11). However, adrenocortical carcinoma as this case is usually included in classification of neuroendocrine tumours (12).

Cancer-related hypercalcemia

In this case hypercalcemia was a paraneoplastic expression which was not caused by bone metastasis as revealed by whole body bone scintigram but most probable by adrenal cancer-derivate PTH related protein (PTHrP) (13). The suppression of

PTH seems consecutive to hypercalcemia while DXA exam was irrelevant for the present circumstance (14). Up to 30% of malignancies associate high serum calcium and it usually represents a poor prognosis (14). PTHrP production or humoral hypercalcemia represents the most common subtype of hypercalcemia but PTHrP is not assessed in daily practice (15,16).

Adrenocortical carcinoma-associated anaemia

In this particular case the clinical presentation a part from abdominal pain and mass was marked by rapidly deterioration of haemoglobin levels. All the hematologic tests showed that the only cause was most probably intra-tumour haemorrhage. The potential alternative mechanisms are: primary adrenal insufficiency in cases with adrenal cancer and contralateral metastases that display more than 90% from adrenal parenchyma, male hypog-

onadism, and bone marrow metastasis (17). Cystic transformation of an adrenal tumour because of the necrosis is possible in adrenocortical carcinoma but it is more frequent in pheochromocytoma, especially in children (18,19).

Poor prognosis of adrenal cancer

The present case introduces a malignant adrenal tumour (although there was not pathological confirmation) with a fatal outcome within days since presentation at Endocrinology Department. Generally a poor prognosis is expected in this type of malignancy despite the progress of technology

and therapy (20). Cortisol producing subtype of adrenal cancer has the highest rate of mortality (as was this case) when compared to the subtypes with other endocrine profile (21).

CONCLUSION

Severe bleeding at the level of the adrenal carcinoma causing symptomatic anaemia is a rare event. The prognosis in adrenocortical carcinoma is poor and the presence of humoral hypercalcaemia represents a sign of short survival time as well as active cortisol production.

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