CASE REPORT

Adrenal incidentaloma caused by extramedullary haematopoiesis: conservative management is optimal

Suganya Sekar,¹ Deepak Burad,² Aby Abraham,³ Mazhuvanchary Jacob Paul¹

¹Department of Endocrine Surgery, Christian Medical College, Vellore, Tamil Nadu, India

²Department of Pathology, Christian Medical College, Vellore, Tamil Nadu, India

³Department of Haematology, Christian Medical College, Vellore, Tamil Nadu, India

Correspondence to
Professor Mazhuvanchary Jacob Paul,
mjpa@cmcvellore.ac.in

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SUMMARY

We present a thalassaemic patient with extramedullary haematopoiesis in the adrenal gland, which is one of the rare sites of involvement. A 29-year-old man presented with a history of anaemia since childhood which required blood transfusion recently. On examination, he had pallor, icterus and splenomegaly with no other palpable abdominal mass. He was diagnosed to have β -thalassaemia. Ultrasonography of the abdomen showed an incidental right adrenal mass with splenomegaly; CT revealed a large right adrenal mass with heterogeneous density. Adrenal adenoma, carcinoma and extramedullary haematopoiesis were considered in the differential diagnosis. After excluding a functioning tumour, the diagnosis was confirmed by ultrasound-guided biopsy. Since the patient was asymptomatic, the adrenal lesion was managed conservatively.

BACKGROUND

Thalassaemia is one of the most common disorders in the Mediterranean region, South and Southeast Asia which leads to extramedullary haematopoiesis. Liver, spleen and paraspinal regions are the usual sites involved. The adrenal as a site of extramedullary haematopoiesis is rarely seen. Conservative management is adequate unless the patient is symptomatic; however, it is unfortunately diagnosed only after adrenalectomy in most cases.

CASE PRESENTATION

A 29-year-old male patient presented with fatigue, decreased effort tolerance intermittently since childhood and a recent history of blood transfusion which he had received during an episode of epistaxis 2 months ago. He had a history of anaemia and jaundice since age 7 and was on iron supplements since then. There was no history suggestive of functioning adrenal tumour. On examination, he was pale, icteric with a blood pressure of 120/80 mm Hg. He had frontal bossing and prominent facial bones. His abdominal examination revealed moderate splenomegaly and no other palpable mass.

INVESTIGATIONS

Laboratory investigations were suggestive of haemolytic anaemia. His haemoglobin was 6.7 g/dL, total white cell count 6100/mm³, platelet count 115 000/mm³, indirect bilirubin 3.1 mg/dL, and his peripheral smear had irregularly contracted microcytic,

hypochromic target cells. Bone marrow biopsy revealed erythroid hyperplasia. The haemoglobin electrophoresis performed was suggestive of β -thalassaemia; the report includes Hb (haemoglobin) A2 4.5% (normal up to 3.5%), fetal Hb 25.5% (normal <1%). He had splenomegaly and a large incidental hypoechoic right suprarenal mass in the ultrasonography of the abdomen (figure 1). On further characterisation by a CT scan, the mass was found to arise from the right adrenal gland of size 8.4×7 cm with heterogeneous density, necrotic changes and a speck of calcification (figure 2).

DIFFERENTIAL DIAGNOSIS

In the background of thalassaemia, the probable diagnosis of extramedullary haematopoiesis (EMH) was made. Functioning adenoma or carcinoma coexistent with thalassaemia was also considered as the differential diagnosis. His biochemical evaluation results are as follows with the corresponding normal values within brackets, 8:00 serum cortisol 13 µg/dL (7–25 µg/dL), overnight dexamethasone suppression test 0.9 µg/dL (up to 1.8 µg/dL), 24 h urinary cortisol 52 µg (10–100 µg), 24 h urinary metanephrines and normetanephrines 111 and 337 µg (up to 350 and 600 µg), and serum potassium 4.3 mmol/L (3.5–4.5 mmol/L); thus, subclinical Cushing's syndrome, pheochromocytoma or Conn's syndrome was ruled out. Ultrasound-guided biopsy reported fibrocollagenous tissue displaying trilineage haematopoiesis. There was erythroid hyperplasia with increase in its immature precursors, and hence the diagnosis of adrenal EMH was confirmed (figure 3).

Figure 1 Ultrasound-guided abdomen showing hypoechoic suprarenal mass.

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Figure 2 CT axial view showing a large right adrenal mass which is heterogeneous with necrotic changes and no invasion of adjacent structures.

TREATMENT

The patient was treated by transfusion with 3 units of packed red cells and the haemoglobin improved to 9.3 g/dL. Treatment with oral hydroxyurea 500 mg once daily and folic acid 5 mg was initiated. The patient was asymptomatic for the adrenal lesion; hence, it was followed up.

OUTCOME AND FOLLOW-UP

At the follow-up visit after 6 months, the patient remained asymptomatic for the adrenal mass.

DISCUSSION

EMH is the formation of haematopoietic tissue outside the bone marrow. It may be physiological, as in the case of a fetus, or it can be pathological when it is associated with various diseases as a compensatory mechanism for ineffective haematopoiesis. Thalassaemia and myelofibrosis are the common associated disorders. Sick cell anaemia, hereditary spherocytosis, chronic myeloid leukaemia and Paget's disease are some of the other disorders which can accompany it. The spleen and liver are the usual sites for EMH; however, other tissues and organs like the adrenal gland, lymph nodes, heart, mediastinum, lung, breast, kidneys, skin, spinal and paraspinal regions, thyroid, gastrointestinal tract and endometrium may also be involved.¹

β -thalassaemia is a wide spectrum clinical disorder with decreased synthesis of β globin chains of haemoglobin. EMH occurs in thalassaemia to compensate for the ineffective

erythropoiesis of bone marrow. Up to 20% incidence of EMH has been reported in patients with thalassaemia.² EMH may be an incidental finding or present with symptoms according to the site involved. It does not require treatment unless symptomatic.¹

The various mechanisms of EMH proposed are stimulation of fetal haematopoietic sites by unknown stimulatory factors, differentiation of pluripotent stem cells to haematopoietic stem cells forming bone marrow elements or embolism of haematopoietic stem cells from extruded bone marrow in an adjacent fracture site.³

The adrenal gland as a site of EMH is described in only a few case reports in the literature. There are no specific diagnostic findings of extramedullary haematopoiesis in imaging studies.⁴ Adrenal EMH may appear as a homogeneous mass in ultrasonography (USG)/CT⁵ or as a heterogeneous mass with cystic change and calcification.⁶ The diagnosis should be confirmed by biopsy after excluding hormonal secretion.

There are published reports of incidentally detected adrenal masses in patients with haematological disorders, where adrenalectomy was performed, resulting in the histological surprise of EMH.⁵⁻⁹ Karami *et al*⁶ reported a patient with clinically palpable asymptomatic adrenal mass, whereas Calhoun *et al*⁷ and Porcaro *et al*⁸ reported patients with incidentally detected adrenal masses on ultrasonography. Lau *et al*⁵ and Banerji *et al*⁹ reported patients presenting with abdominal pain and found to have adrenal masses on imaging. All these patients remained undiagnosed after imaging or biochemical evaluation and underwent diagnostic adrenalectomy.

Chuang *et al*¹⁰ reported a patient with thalassaemia who presented with a palpable mass in the right upper abdomen; the diagnosis of adrenal EMH was made after surgical exploration and intraoperative biopsy permitting conservative management by leaving the tumour in situ.

There are two reports in the literature of patients diagnosed by image-guided biopsy avoiding adrenalectomy or open biopsy. King *et al*¹¹ reported incidental bilateral adrenal enlargement on CT in a patient with myeloid metaplasia diagnosed to have EMH by CT-guided biopsy and managed conservatively. Keikhaei *et al*¹² reported an incidental adrenal mass on ultrasonography of the abdomen for splenomegaly in a patient with thalassaemia; EMH was diagnosed by USG-guided biopsy and the patient was managed conservatively.

Additionally, Wat *et al*¹³ reported non-invasive diagnosis and conservative management of bilateral incidental adrenal masses in a patient with thalassaemia; EMH was suggested by uptake of technetium 99 m nano colloid scintigraphy.

Figure 3 H&E stain $\times 40$ section showing trilineage haematopoietic cells with erythroids, myeloids and megakaryocytes.

Learning points

- ▶ Adrenal extramedullary haematopoiesis (EMH) must be remembered as an important cause of an incidental adrenal mass in the setting of haematological disorders.
- ▶ Since there are no specific image characteristics for adrenal EMH, evaluation to rule out functioning adenoma is required before attempting a biopsy.
- ▶ The surgical morbidity of adrenalectomy can be avoided if this differential diagnosis is remembered and image-guided biopsy is used to clinch the diagnosis.
- ▶ It is prudent to follow-up these patient without any intervention unless symptomatic.

Blood transfusion and hydroxyurea (a ribonucleotide reductase enzyme inhibitor) can be used as initial medical management; hydroxyurea stimulates the synthesis of fetal haemoglobin, thereby decreasing ineffective haematopoiesis. Radiotherapy up to 4.5 Gy has been used with good results in symptomatic patients. Surgical excision is recommended in patients who are symptomatic and resistant to other modalities.^{1 2}

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