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## Adrenal extramedullary hematopoiesis in the setting of anti-Diego antibody and congenital dyserythropoietic anemia

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### Abstract

Extramedullary hematopoiesis occurs in the setting of hematologic disorders or malignancies when the activity of the bone marrow is insufficient to generate blood cells. We report a unique case of adrenal extramedullary hematopoiesis diagnosed in a 16 year old female with a history of anti-Diego antibody and congenital dyserythropoietic anemia. She presented with an enlarging adrenal mass and underwent surgical resection. Pathology revealed extramedullary hematopoiesis. On literature review, we identified only two prior existing cases of adrenal extramedullary hematopoiesis in pediatric patients, with no prior case reports of adrenal extramedullary hematopoiesis occurring in patients with anti-Diego antibody or in those with congenital dyserythropoietic anemia.

### Keywords

Adrenal extramedullary hematopoiesis; anti-Diego antibody; Congenital dyserythropoietic anemia

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#### Author contributions

Julson was involved in literature review and manuscript preparation. Mroczek-Musulman analyzed pathological specimens. Hilliard provided guidance with manuscript preparation. Beierle provided senior guidance with manuscript preparation. All authors attest that they meet the current ICMJE criteria for Authorship.

#### Consent

Consent to publish the case report was not obtained. Our institution is exempt from the requirement of an IRB for a case report.

#### Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Janet Rae Julson reports financial support was provided by National Institute of Health. Janet Rae Julson reports a relationship with National Institute of Health that includes: funding grants.

## 1. Introduction

Hematopoiesis occurs in the liver, spleen, and lymph nodes in the fetus, and ultimately transitions to the bone marrow in adults. These fetal sites of hematopoiesis are the most common sites of extramedullary hematopoiesis in the adult. Extramedullary hematopoiesis occurs in the setting of various hematologic disorders or malignancies including sickle cell disease, thalassemias, and myelodysplastic syndromes amongst other conditions when the bone marrow is unable to generate sufficient blood cells [1,2]. Here, we present a unique case of adrenal extramedullary hematopoiesis presenting as an enlarging adrenal mass in a patient with a history of anti-Diego antibody and congenital dyserythropoietic anemia.

## 2. Case report

Patient is a 16 year old Hispanic female with cerebral palsy and a past hematologic history notable for anti-Diego antibody and congenital dyserythropoietic anemia. She had undergone an ultrasound and magnetic resonance imaging (MRI) of the liver to evaluate transaminitis, and a 3.4 × 4.0 × 3.5 cm heterogeneous solid right adrenal mass was incidentally noted. Labs, including urine homovanillic and vanillylmandelic acid, serum cortisol, aldosterone, and catecholamines were all within normal limits. This mass was followed with serial imaging and ultimately, over the course of one year, enlarged to 5.2 × 4.3 × 4.8 cm and obliterated the right adrenal gland (Fig. 1 A). Based on these changes, the child's care team decided to proceed with surgical resection. She underwent laparoscopic right adrenalectomy. Grossly the lesion crowded the normal adrenal gland (Fig. 1 B). Histology revealed polymorphic proliferation of hematopoietic precursors including myeloid, erythroid, and megakaryocyte precursor cell lines suggestive of extramedullary hematopoiesis (Fig. 1 C, D).

## 3. Discussion

While there are case reports in the literature of adrenal extramedullary hematopoiesis in the adult population, there are only two such documented cases in pediatric patients. Porcaro et al. described a 10 year old Caucasian female with a history of beta-thalassemia who, similarly to our patient, had an incidentally identified right adrenal lesion and underwent adrenalectomy with pathology revealing extramedullary hematopoiesis [3]. Calhoun et al. presented the case of a 9 year old male with a history of hereditary spherocytosis found to also have a right adrenal lesion as part of a workup for jaundice [4]. He underwent partial right adrenalectomy and pathology was consistent with extramedullary hematopoiesis.

There are no documented case reports of extramedullary hematopoiesis in patients with Diego blood antigens. The Diego blood group system was first described in 1955 when it was found to cause fatal hemolytic disease of the newborn [5]. There are a total of 22 antigens within the system and their impacts range from clinical insignificance to hemolytic transfusion reactions, as seen in our patient, or to hemolytic disease of the newborn [6]. In adult case reports, adrenal extramedullary hematopoiesis has been reported in patients with thalassemia [7–16], sickle cell disease [17], primary myelofibrosis [18], and myeloid

metaplasia [19] The discovery of a patient with Diego blood antigens in this setting is a unique finding within the existing literature.

In regards to our patient's past medical history of congenital dyserythropoietic anemia, this diagnosis includes a family of anemias which lead to hemolytic anemia secondary to the inappropriate synthesis of the erythroid cell line [20] Heimpel et al. reported twelve cases of paravertebral extramedullary hematopoiesis in adult patients with a history of congenital dyserythropoietic anemia [21] There are several other case reports in the literature of paravertebral and mediastinal extramedullary hematopoiesis, but on our review there were no documented cases of adrenal extramedullary hematopoiesis in adult or pediatric patients with congenital dyserythropoietic anemia [22,23].

There are at least three case reports in the literature of adult patients with past medical history of hematologic disorders, two with thalassemia and one with myeloid metaplasia, and incidentally discovered adrenal masses who underwent image-guided biopsy which demonstrated extramedullary hematopoiesis and subsequently avoided adrenalectomy [13,19,24]. Because of our patient's anti-Diego antibodies and its associated difficulties obtaining compatible blood products, we chose to proceed with surgical resection in the situation of increasing size of the adrenal mass in lieu of a percutaneous biopsy with potential for hemorrhage and subsequent need for transfusion.

In summary, we have presented a rare case of pediatric adrenal extramedullary hematopoiesis and more uniquely, the first documented case of adrenal extramedullary hematopoiesis in a patient with anti-Diego antibody and congenital dyserythropoietic anemia. Extramedullary hematopoiesis should be considered in the differential diagnosis of adrenal masses in children with hematologic disorders when workup for functional tumors is negative.

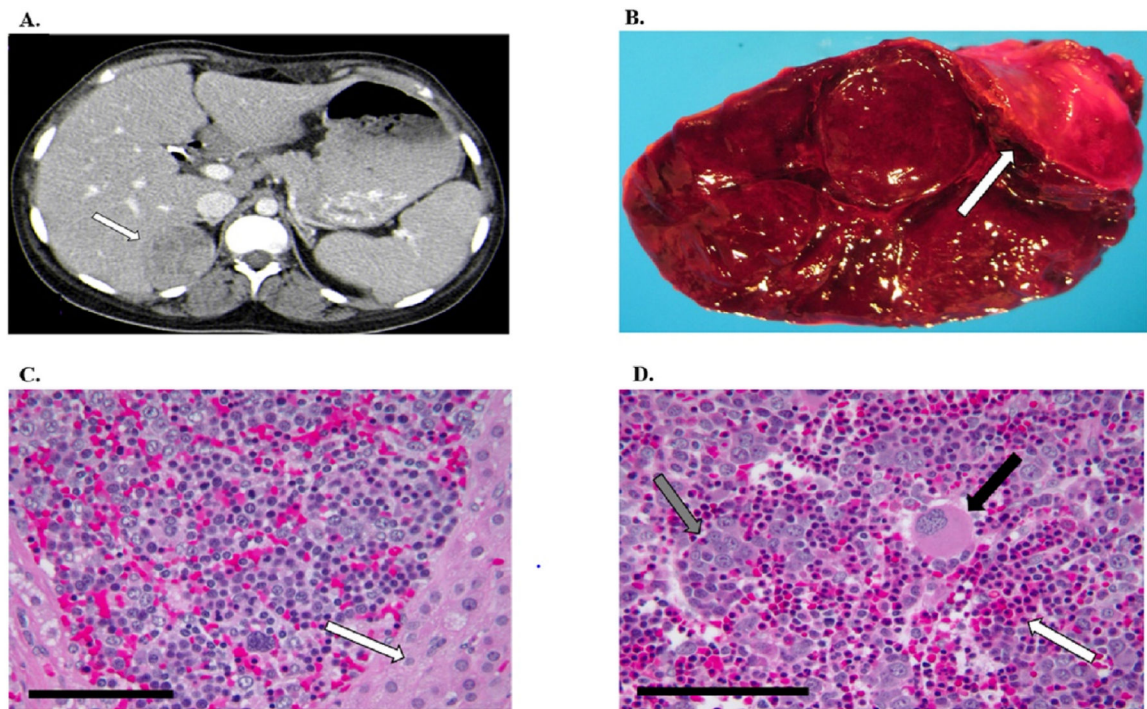
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**Fig. 1.** Imaging and pathology of adrenal mass. (A) Computerized tomography demonstrated a  $5.2 \times 4.3 \times 4.8$  cm mass obliterating the right adrenal gland (*white arrow*). (B) Photo of gross cross-section of right adrenal mass demonstrating adrenal tissue (*white arrow*) crowded by extramedullary hematopoiesis (C) Photomicrograph of hematoxylin and eosin staining showing normal adrenal tissue (*white arrow*) surrounded by hematopoietic precursors (10 $\times$  magnification, scale bar represents 0.3mm) (D) Photomicrograph of hematoxylin and eosin staining demonstrating higher power view (40 $\times$  magnification, scale bar represents 0.1mm) of hematopoietic precursors including megakaryocytes (*black arrow*), myeloid precursors (*gray arrow*), and erythroid precursors (*white arrow*).