Journal of Taibah University Medical Sciences (2016) ■(■), 1–4

Taibah University

Journal of Taibah University Medical Sciences

www.sciencedirect.com

Case Report

Hereditary protein C deficiency in a Saudi neonate with bilateral adrenal gland haemorrhages: A rare case report

Zakaria M. Al Hawsawi, MD [a,*], Amal A. Alhejaili, MBBS [b], Moeen Mohy Uddin, MD [c] and Mohamed E. Abdelkarim, MD [d]

[a] *Paediatric Department, Medina Maternity & Children's Hospital, College of Medicine, Taibah University, Almadinah Almunawwarah, KSA*
[b] *Paediatric Department, Medina Maternity & Children's Hospital, Almadinah Almunawwarah, KSA*
[c] *Paediatric Department, Al-Dar Hospital – Almadinah Almunawwarah, Almadinah Almunawwarah, KSA*
[d] *Department of Radiology, Medina Maternity & Children's Hospital, Almadinah Almunawwarah, KSA*

Received 27 January 2016; revised 12 March 2016; accepted 17 March 2016; Available online ■ ■ ■

الملخص

يُعنى هذا التقرير بطفلة سعودية نتاج حمل كامل، تبلغ من العمر أربعة أيام، وتم تشخيصها بالنقص الوراثي لبروتين "ج"، وكانت مراجعتها للمستشفى نتيجة نزف في الغدتين الكظريتين، ونزف داخل الجمجمة والفُرفُرية الخاطفة. الطفلة هي نتيجة الحمل الأول لوالدتها بعد حمل اعتيادي، لوالدين بينهما قرابة نسب. ولم تظهر على والديها أعراض نقص بروتين "ج". أثناء العلاج توقف نزف الغدة الكظرية، إلا أنها أصيبت بالاستسقاء الدماغي، الذي نتج عنه الشلل الدماغي. تم علاج ذلك بداية بالبلازما الطازجة المجمدة ثم وقائيا بالهيبارين منخفض الوزن الجزيئي. لم يسبق نشر حالة مماثلة تعاني من الجمع بين نقص بروتين "ج" ونزف الغدة الكظرية في حديثي الولادة، ويبدو أن هذا التسجيل هو الأول من نوعه. على الرغم من أن نقص بروتين "ج" قد يكون مكتسبا، إلا أن الحالة موضوع الدراسة أثبتت أنها عيب وراثي متماثل الألائل. هناك الحاجة للمزيد من الدراسات الجينية للتعرف على أسباب هذا الترابط النادر.

الكلمات المفتاحية: نقص بروتين ج؛ نزف الغدة الكظرية؛ حديث ولادة سعودي مصاب بنزف داخل الجمجمة

Abstract

This case report describes a full-term 4-day-old Saudi new-born girl diagnosed with hereditary protein C deficiency, who presented with bilateral adrenal gland haemorrhages, intracranial haemorrhage and purpura fulminans. She was born to a consanguineous couple after an unremarkable pregnancy involving a primigravida mother. Her parents were asymptomatic for protein C deficiency. During treatment, her adrenal haemorrhage resolved, but she developed hydrocephalus complicated by cerebral palsy that was initially treated with regular fresh frozen plasma (FFP) and later by low-molecular-weight heparin prophylaxis. Association of protein C deficiency and adrenal haemorrhage in neonates has not been reported previously, and this appears to be the first such case report of its type. Although protein C deficiency may be acquired, the case under consideration proved to be a homozygous hereditary defect. Further genetic studies are required to identify the aetiology of this rare association.

Keywords: Adrenal gland haemorrhage; Protein C deficiency; Saudi neonate with intracranial haemorrhage

* Corresponding address: Medina Maternity & Children's Hospital, Taibah University, P.O. Box: 6205, Almadinah Almunawwarah, KSA.
E-mail: zhawsawi@yahoo.com (Z.M. Al Hawsawi)

Peer review under responsibility of Taibah University.

ELSEVIER Production and hosting by Elsevier

Introduction

Protein C (PC) is a vitamin K-dependent protein synthesized in the liver. PC has a molecular weight of approximately 62 kDa, and the gene is located on human chromosome 2 and appears to be closely related to the gene

1658-3612 http://dx.doi.org/10.1016/j.jtumed.2016.03.004

Please cite this article in press as: Al Hawsawi ZM, et al., Hereditary protein C deficiency in a Saudi neonate with bilateral adrenal gland haemorrhages: A rare case report, Journal of Taibah University Medical Sciences (2016), http://dx.doi.org/10.1016/j.jtumed.2016.03.004

for factor IX.[1,2] It was first described in 1981.[3] A deficiency in PC is one of several hereditary abnormalities of haemostasis that have been described in patients at high risk for thromboembolic complications. The disease is usually inherited as an autosomal dominant trait. The main clinical presentation features in the neonatal period are PF and intracerebral haemorrhage, which present shortly after birth; therefore, we are reporting a case of PC deficiency in a Saudi neonate with bilateral adrenal haemorrhages along with intercerebral haemorrhage and purpura fulminans. Our objective in this report is to describe this rare disease and very rare association that has not been previously reported in a neonate.

Case report

We describe this rare case of a term female with homozygous PC deficiency that led to bilateral adrenal haemorrhages, intracranial haemorrhage and purpura fulminans.

She was born by emergency Caesarean section because of foetal distress to a 26-year-old healthy primigravida mother with a consanguineous marriage. She had poor respiratory effort and a weak cry requiring bag and mask ventilation for less than one minute. The neonate had an Apgar score of 7 and 9 at 1 and 5 min, respectively. She was admitted to the neonatal intensive care unit because of mild respiratory distress. Her initial blood gas showed metabolic acidosis that resolved without any treatment. Her complete blood count revealed a haemoglobin (Hgb) level of 17.6 g/dl, a white blood cell count (WBC) of 26.9000/mm^3, haematocrit (Hct) of 53.4% and a platelet count of 62.000/mm^3. Her urea and electrolytes were normal. She was started on intravenous antibiotics that were discontinued following negative blood cultures at 72 h of life.

However, her aspartate transaminase (AST) was 505 u/L, alanine transaminase (ALT) was 627 u/L and total bilirubin (TSB) was 125 μmol/L. A brain ultrasound on day 2 showed bilateral intracerebral haemorrhages along with a grade 4 intraventricular haemorrhage, which was confirmed by a CT scan on day 4 (Figure 1). Her oxygen saturation was maintained on room air, and her liver function tests improved. However, her Hct suddenly dropped from 43% to 28%, suggestive of possible blood loss. An abdominal ultrasound performed to assess possible blood loss in the abdomen showed bilateral adrenal haemorrhages (Figures 2–3).

She received a blood transfusion and repeated infusions of FFP. On day 10, she developed haemorrhagic necrotic skin lesions on the medial aspect of the right thigh and left forearm with some scattered purpuric lesions over her lower abdomen. All her peripheral pulses and blood pressures were normal. Neonatal purpura fulminans was suspected, and replacement therapy with FFP (10 ml/kg) was initiated every 12 h. Although there was no family history of venous thrombotic disease, a diagnosis of protein C deficiency was considered by the haematologist, and a workup was performed for the baby and her parents. The patient's protein C antigen level was 24% (reference range 70–140%). (Protein C level measurement was performed on a Siemens DBC-XP machine using an optical method.) The mother's protein C level was 46%, and the father's level was 52%. The protein S

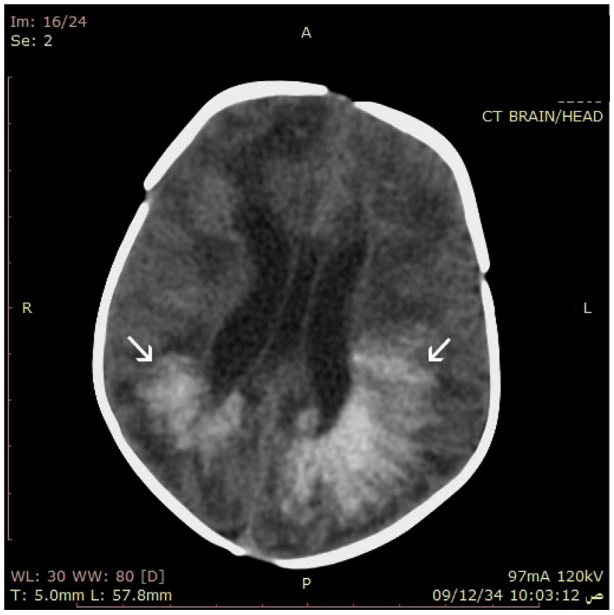

Figure 1: Unenhanced axial brain CT scan shows bilateral cortical and subcortical hyperattenuating lesions indicating haemorrhage (arrows).

level was normal in the infant. Her coagulation profile and clotting factors were normal, and the patient received vitamin K at birth. A follow-up ultrasound of the abdomen showed resolution of the adrenal haemorrhages at 2 months of age, and the repeated protein C level was 4% at that time. A follow-up brain MRI showed bilateral hydrocephalus (Figure 4), for which a ventriculoperitoneal (VP) shunt was placed. She developed signs of cerebral palsy with developmental delay as a sequela of the intracranial haemorrhage and hydrocephalus. At 5 months of age, her right eye was noted to be smaller than the left one. An evaluation by an ophthalmologist revealed a retinal detachment secondary to an organized vitreous haemorrhage. The patient was maintained on twice weekly FFP that controlled her recurrent purpuric lesions. At 11 months of age, she was shifted to low-molecular-weight heparin. She also received follow-up care from a physical therapist and a neurosurgeon for rehabilitation and hydrocephalus management, respectively.

Discussion

The main function of PC is its anticoagulant property as an inhibitor of coagulation factors V and VIII. PC deficiency results in a loss of the normal cleavage of factors Va and VIIIa. Due to the dominant inheritance pattern of the disease, the majorities of people with protein C deficiency lack only one of the functioning genes and are therefore heterozygous. Patients with *homozygous* protein C deficiency have two abnormal copies of the gene, leading to the absence of functioning protein C in the bloodstream.

The heterozygous type of PC deficiency is inherited in an autosomal dominant fashion in some families. The clinical presentation of the heterozygous form of the disease is usually of venous thromboembolism in adolescent and adult

Please cite this article in press as: Al Hawsawi ZM, et al., Hereditary protein C deficiency in a Saudi neonate with bilateral adrenal gland haemorrhages: A rare case report, Journal of Taibah University Medical Sciences (2016), http://dx.doi.org/10.1016/j.jtumed.2016.03.004