CASE REPORT

Per Oral Bleeding: Rare Presentation of Gardner-Diamond Syndrome

Unaiza Qamar, Nisar Ahmad and Saima Farhan

ABSTRACT

A 10-year boy presented with spontaneous episodes of oral bleeding for the last 6 months. Detailed ENT examination showed no pathology, bleeding profile was normal, endoscopy and dental examination also did not reveal any abnormality. Child abuse or malingering was also ruled out. Initially the child was managed with platelet transfusion and fresh frozen plasma and then put on follow-up treatment with antifibrinolytics, Vitamin C but the episodes became recurrent. Psychiatric evaluation revealed that child was suffering from depression. Antidepressants were prescribed by the psychiatrist that not only cured the depression with time but also the bleeding episodes which were actually related to child's depression (Gardner-Diamond syndrome or psychogenic purpura). This is a diagnosis by exclusion where the patients bleed due to dysregulated steroid secretion secondary to stress; resulting in development of sensitization to RBC membrane, and dysregulated fibrinolytic system activity.

Key Words: *Gardner-Diamond syndrome. Autoerythrocyte sensitization. Psychogenic purpura. Haemostasis.*

INTRODUCTION

Haemostatsis is defined as a process through which blood coagulation is started and completed in a rapid and steady managed style.[1] When various laboratory tests aimed at testing haemostasis are invariably normal then pscychogenic causes, child abuse and malingering need to be ruled out[2,3] and sometimes stress itself can lead to haemostatic defects since central nervous system, immune system, vessels and fibrinolytic system are closely integrated.[4]

We are presenting a case of a 10-year boy who was referred to Children's Hospital, Lahore, for evaluation of per oral bleeding for which no cause was found. To rule out the possibility of child abuse, he was referred to Psychiatry Department and it was found that the child was depressed. To the best of our knowledge this is the first such case of bleeding tendency related to anxiety/depression reported in our part of the world.

CASE REPORT

A 10-year boy presented to Children's Hospital, Lahore, with complaints of per oral bleeding for one month. A month back the patient developed haematemesis consisting of fresh blood that was a cup in quantity, epistaxis and bleeding gums. He was rushed to a local hospital where during his stay he was given fresh frozen plasma, Tranexamic Acid and one platelet transfusion. Bleeding stopped and patient was discharged on Viatmin C and capsule Tranexamic Acid. But these episodes became recurrent and would occur every 5-6 days. There was no past history of bleeding. The child was a product of non-consangineous marriage with no family history of any bleeding disorder. The systemic examination was unremarkable.

Investigations for bleeding disorder i.e. CBC, PT/APTT, bleeding time and thrombin time were repeatedly performed and found to be normal. Mild factor deficiencies, factor XIII defieciency, mild Von Willebrand disease and platelet function defects were investigated. FXIII assays, vWF: Ag, platelet aggregation studies with ADP, epinephrine, collagen and ristocetin assays were all normal while α_2 antiplasmin assays could not be performed due to non-availability and the age at presentation. Liver, renal and immunological profile were normal as well. Viral studies for hepatitis B and C and Dengue IgM and IgG were negative. Ear, nose, throat and dental pathologies were also ruled out by the respective departments. Chest X-ray, esophageal and gastric endoscopy revealed no abnormalities.

The patient was then referred to the Department of Psychiatry. Psychiatric evaluation ruled out any possibility of child abuse or any possibility of a motive behind inflicting child with injuries. The patient academically seemed to be slow and not enjoying his school activities with mild distress at home as well, the nature of which cannot be revealed in respect of the patient's confidentiality. Father reported some link between bleeding episodes and academic stress. On general look, the child was anxious with poor eye contact during conversation. IQ test was advised to evaluate his learning abilities. There was a lag of 2 years in learning capacity for his age which led to difficulties to

Department of Haematology, Children's Hospital and Institute of Child's Health, Lahore.

Correspondence: Dr. Unaiza Qamar, 72 Neelam Block, Allama Iqbal Town, Lahore.
E-mail: unaiza.qamar@gmail.com

Received: July 10, 2012; Accepted: August 26, 2014.

cope up with his studies. He was put on Tab. Nortriptyline (antidepressant) by the psychiatry department. The therapy was initially aimed at treating his anxiety. With time not only his depression alleviated but also his bleeding tendency subsided.

Autoerythrocyte sensitization test, where patient's own RBCs were injected intradermally into his forearm, was performed which led to induration at the injection site 48 hours later, thus further strengthening the diagnosis of Gardner-Diamond syndrome. Psychiatric therapy was then gradually and successfully diminished and this coupled with good re-assurance led to gradual cessation of symptoms and now the patient is having no further complaints of bleeding episodes from anywhere.

DISCUSSION

Gardner-Diamond syndrome was described by Louis Gardner and Frank Gardner in 1955. They described four Caucasian women who developed painful ecchymotic lesions for which all the work-up was normal and there was no history of any self inflicted wounds or any abuse. The underlying pathology was later found out to be autosensitization to RBC membrane stroma especially phosphatidylserine.[5] Only about 120 cases have been described in literature to date. These patients at first glance appear to be quiet, shy, pleasant, and seemingly well-adjusted but on careful probing are often found to have extremely abnormal backgrounds.[6] This goes for our patient too.

Patients present with unexplained painful ecchymotic lesions or unexplained bleeding. Caucasian women are particularly vulnerable, but men and children are no exception. The condition is precipitated by emotional stress and affected individual generally have psychiatric co-morbidities.[6] It is very rightly called a medical mystery.[5]

Gardner-Diamond syndrome is not uncommon in paediatric population and it can be confused with child abuse.[7] But because of the rarity of the disorder, there are few methods of support in place for diagnosis. Gardner-Diamond syndrome is always a diagnosis of exclusion. Diagnosis is mainly clinical and one has to have a very high index of suspicion. Supporting evidence in literature includes ruling out local pathologies, normal haemostasis work up, presence of psychiatric co-morbidities and response to psychiatric therapy. The only investigation mentioned in the literature which has been of help, though not confirmatory, is autoerythrocyte sensitization test where patient's own red blood cells injected intradermally lead to induration ater 24 - 48 hours.[6,8] This patient fulfilled all the above criteria since the bleeding episodes have had a relationship with the stress; all the exhaustive work-up performed was normal, the autoerythrocyte sensitization test led to induration at the injected site. There was a remarkable response to the psychiatric treatment and since then he has never had the same complaint again.

Gardner and Diamond believed that the syndrome was due to autosensitization to RBC membrane.[5] The concept of psychoimmunology is the latest etiological hypothesis. According to this concept we have an intricate neuroimmunocutaneous endocrine network. During stress, communication between the brain and the immune system mediated by neuropeptides sets-up a vicious cycle resulting in sensitization to one's own RBC membrane stroma, the result of which is autoimmune vasculopathy and dysregulated activity of tissue plasminogen activator in the skin leading to unabated fibrinolysis. Based on this hypothesis autoerythrocyte sensitization test was devised by Ratnof. Although it is not standardized or commercially available, but if induration develops, this is the only positive finding.[6]

Since Gardner-Diamond syndrome is a chronic unexplained medical condition, to deal with it an organized approach is indispensible with effective communication between haematologist and psychiatrist.[5] Treatment of underlying psychiatric disorder stays the mainstay of treatment. Pain control with Amitriptyline and Promethazine can be offered. Although no clinical trials are there but there have been case reports in which patients were benefitted from plasmapheresis.[9]

The prognosis of Gardner-Diamond syndrome is good with no deaths reported from this syndrome or its complications. Relapses at the time of severe emotional stress are very common.[6] Having an awareness of this rare condition will assist in the prevention of unnecessary investigations.

REFERENCES

1. Kumar V, Abbas AK, Faousto N, editors. Robbins and Cotran pathologic basis of disease. 7th ed. Philadelphia: *Elsevier;* 2005.
2. Vun YY, Muir J. Periodic painful purpura: fact or factitious? *Australas J Dermatol* 2004; **45**:58-63.
3. Vasinova M. Ethical dilemmas in pediatrics. *Med Law* 2000; **19**:569-89.
4. Hedrick HL, Nelson RM. Handling ethical conflicts in the clinical setting. *Semin Pediatr Surg* 2001; **10**:192-7.
5. Gardner FH, Diamond LK. Autoerythrocyte sensitization: a form of purpura producing painful bruising following auto-sensitization to red blood cells in certain women. *Blood* 1955; **10**: 675-90.
6. Ivanov OL, Lvov AN, Michenko AV, Künzel J, Mayser P, Gieler U. Autoerythrocyte sensitization syndrome (Gardner-Diamond syndrome): review of the literature. *J Eur Acad Dermatol Venereol* 2009; **23**:499-504.
7. Bostwick JM, Imig MW. Gardner-Diamond syndrome: bruising feeling. *Mayo Clin Proc* 2008; **83**:572.
8. Geisler BP, Dezube BJ. Psychogenic purpura (Gardner-Diamond syndrome) [Internet]. 2011. Available from: http://www.uptodate.com/contents/psychogenic-purpura-gardner-diamond-syndrome
9. Meeder R, Bannister S. Gardner-Diamond syndrome: difficulties in the management of patients with unexplained medical symptoms. *Paediatr Child Health* 2006; **11**:416-9.