International Journal of Health Sciences and Research
www.ijhsr.org ISSN: 2249-9571

Case Report

Acquired Platelet Dysfunction with Eosinophilia: A Report of 3 Cases with Review of Literature

Brij Mohan Kumar Singh[1], Annamma Kurien[2], Barnini Banerjee[3], Elcid Vijay Kumar[4]

[1,2]Department of Pathology, Melaka Manipal Medical College, Manipal Campus, Manipal University.
[3]Department of Microbiology, Kasturba Medical College, ManipalUniversityManipal
[4]Department of Clinical Laboratory and Hematology, Kasturba Hospital, Manipal University Manipal.

Corresponding Author: Brij Mohan Kumar Singh

Received: 09/06//2014 *Revised: 06/07/2014* *Accepted: 10/07/2014*

ABSTRACT

Patients who were in good health, with no history of any drug ingestion or recent travel, presented with spontaneous widespread bruising and ecchymosismainly on the extremities. No history of severe bleeding was noted. These patients on laboratory evaluation did not show any abnormalities in basic hemostatic screen with BT (Bleeding Time), CT (Clotting time), PT (Prothrombin Time), APTT (Activated partial thromboplastin time) and platelet count. None of these patients were having parasitic infestation. Only on direct smear (without anti-coagulant) it was noticed that they have increased eosinophil count and showing abnormal platelet morphology. On Aggregation study they show reduced aggregation with all the agonist (ADP, Epinephrine, Archidonic acid, and Collagen). Normal aggregation pattern was observed with Ristocetin. These changes in platelet function and morphology may be due to acquired storage pool disorder of the platelets termed as APDE (Acquired platelet dysfunction with eosinophilia).

Key word: APDE (Acquired Platelet dysfunction with eosinophilia), Eosinophil, Platelets

INTRODUCTION

Bleeding in the form of ecchymosis and purpura are taken into serious consideration when it occurs spontaneously, that is without any trauma. Most of the time these bleeding episodes are related in to somekind of coagulation defect in the body. But many a time, these bleeding tendencies occur in the absence of the deadly coagulation disorder. They are attributed sometimes to a functional disorder of the platelets, despite normal number of platelets in the blood. Among the many known causes of acquired form of bleeding in the skin and mucous membrane, anincreased eosinophil count is one of the established factor which causes petechiae, purpura and ecchymosis; resulting in the functional disability of the platelet in the formation of primary platelet plug. This is a transient state of platelet dysfunction which is accompanied by a marked eosinophilia known as APDE (Acquired platelet dysfunction with eosinophilia). Almost all cases have been reported from South East Asian countries because of the fertile grounds for the eosinophil count to go up in the blood.

Historical Sketch

Acquired platelet dysfunction with eosinophilia or non-thrombocytopenic purpura with eosinophilia is an acquired form of platelet disorder with unknown etiology first reported by Mitrakul [1] and Suvatte [2] in 1975, from South East Asian countries. After Mitrakul in the year 1977, Israngkula [3] took the initiative and named this disease as "Acquired platelet disorder with eosinophilia" (APDE) and described the abnormal forms of platelets seen in this disease.

Demography

often the cause of eosinophilia in the patients from south east Asian countries are parasitic infestation which arefurther much more common in pediatric age group. There are few such cases which are reported in the western world. [4,5] Untill now, all the cases of APDE were reported from the countries like Thailand, Malaysia, and Singapore. These cases which are very unique in their own presentation that these children are of the age group of 5-8 years of age and are reported in countries like United Kingdom and Canada. These children have a recent history of travel to Indonesia five months before consultation, these children presented with unprovoked petechial rash and bruises.

Most of the studies indicated the helminthic infestation as the cause of this platelet dysfunction, but how these helminths would explain the geographic occurrence is still mysterious. [6]

CLINICAL PRESENTATION

The clinical presentation of the patients with APDE is very distinct with either ecchymosis or purpuric patch over the body with no organomegaly. Most of the time, the patient presents in their childhood, mainly 1-12 years of age but adult and adolescent groups are also not spared. There are no literaturereport which suggest the involvement of older age group by this type of bleeding diathesis. Both the sexes are equally affected. Sometimes these patients can also present with mucosal bleeding with or without purpural rash or other skin manifestation. These patients with the exception of bleeding manifestation, are in relatively good health with no past history of any bleeding in the patients or in the family. It should be noted at this juncture that bleeding due to certain drug intake which can cause platelet abnormalities should be sought from a detailed drug history.

Laboratory Investigation

Eosinophilia is found in all cases of APDE which persists for few months after the onset of bleeding manifestation. The eosinophil count varies from 11-70% of total WBC count.

This thrombocytopathic bleeding disorder is characterized by a prolonged bleeding time, positive Hess's test, degranulated platelet, and most important, abnormal platelet aggregation tests, suggesting a platelet storage pool disorder.

Mild leukocytosis can also be found in 80% of the cases. [3] Eosinophilia with mild leukocytosis in a patient is sometimes a very transient episode and if the patient presents with the bleeding symptoms a few weeks after onset, eosinophilia may not be present.

Quantitatively platelets may be adequate or low normal in number for the age but, morphologically platelets when stained with leishman stain shows pale staining, fewer granules(Fig 3) in the cytoplasm, intact well delineated cell membrane and reduced or absent platelet aggregates on direct smear (without anticoagulant). These abnormal morphologic features are usually seen in 30-80% of total platelets in blood smear. [3,7] The amount of abnormal morphology is directly proportional to the severity of bleeding manifestation. [8] It is also seen, that as the patient recovers from eosinophilia and

symptoms improves or recover, platelet abnormalities decrease or become normal.

Bleeding time is prolonged in about 60% of cases, [2,8] Clot retraction is normal in all the cases. [8]

Platelet factor 3, release is abnormal in 50% of the patients. [2] Immunoglobulin are in normal range including IgG, IgA, IgM, however, IgE is increased in variable amount.Stool examination in most of the cases show common parasite , e.g. Ascaris, Hookworm, Enterobius, etc. in 50-60% of the cases. [2] Platelet aggregation studies in almost all cases show decreased aggregation in response to ADP, thrombin and collagen, but the response to ristocetin is normal. [2,8]

Pathogenesis

The exact mechanism of this phenomenon is still not clear but few theories suggest that high IgE levels in response to parasitic infestation causes mast cell degranulation and leads to an in-vivo platelet activation.

Management

Most of the cases with acquired platelet dysfunction with eosinophilia (APDE) resolve by themselves with the decrease in the eosinophil count. Most of them have definite causes of eosinophilia such as patients' stool examinations are positive of various parasites. In one of the largest study done by Suvatte et al, [2] 58% of the stool samples were positive for parasites, particularly *Ascaris, Enterobius* and *Ankylostoma.*

It becomes very important to recognize the benign nature of this illness which masquerade idiopathic thrombocytopenic purpura like symptoms and patient may undergo various unnecessary investigations.

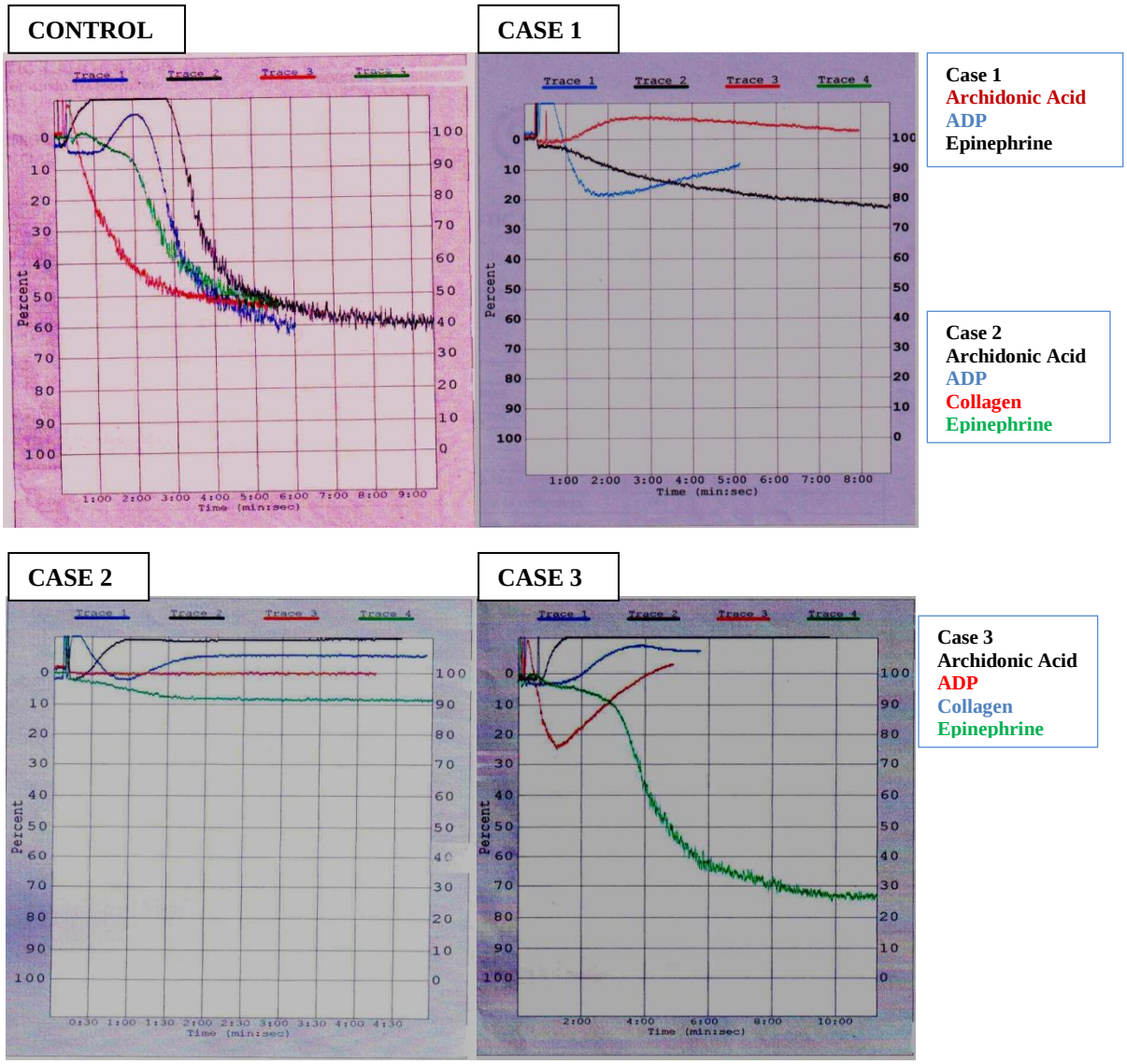
CASE REPORT

Summary Of Cases

CASE	AGE/SEX	PARASITOLOGY FINDINGS	FAMILY HISTORY	CLINICAL FEATURE	RECOVERY
Case 1	11month/Male	No parasite recovered	Born from a consanguineous marriage	Easy bruisability, ecchymotic patches	Recovered in 3 months
Case 2	30 years/Male	No parasite recovered	NIL	Ecchymotic Patches	Recovered in 5 months
Case 3	4 years/Male	No parasite recovered	NIL	Recurrent ecchymosis	Recovered in 2 months

The results of patients' platelet aggregation tests

TEST	CASE 1(%)	CASE 2(%)	CASE 3(%)
ADP Patient/control	21/50	14/65	23/58
Epinephrine(10µM) Patient/control	21/68	08/60	64/57
Archidonic Acid(0.5mM/ml) Patient/control	02/83	03/79	01/56
Ristocetin (1.5mg/ml) Patient/control	105/99	82/83	89/64
Ristocetin (0.5mg/ml) Patient/control	03/03	1/0	0/0
Collagen(2µg/ml) Patient/control	-	02/62	02/61



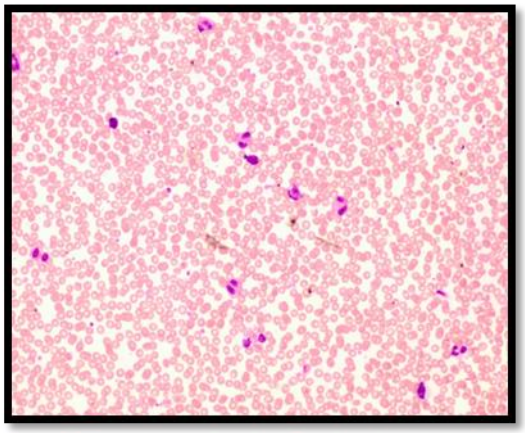


Fig 1: Direct smear. Leishman stain X200. Eosinophils

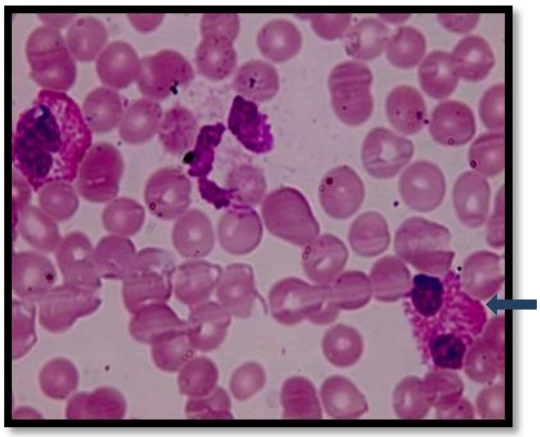


Fig 2: Direct smear. Leishman stain X1000. Eosinophils

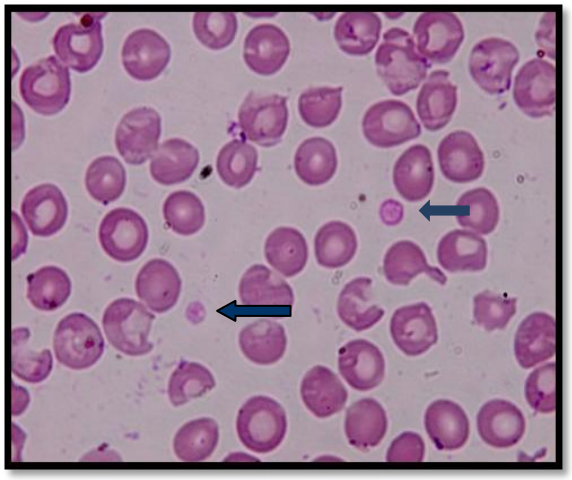


Fig 3: Direct smear. Leishman stain X400. Pale staining of platrelets and hypogranularity.

All of the children in the present study were in good health and had no history of any drug ingestion. All the 3 cases had widespread spontaneous ecchymosis specially on the upper limb and trunk. No history of severe bleeding were detected in any cases. The number of platelets in all the cases was within normal limits but the platelet morphology was abnormal in all cases, platelets werehypogranular(Fig 3). Eosinophilia was detected in all these cases. These patient were subjected for hemostatic work up including Bleeding Time (BT), Prothrombin Time (PT), Activated partial thromboplastin time(APTT), Thrombin Time (TT), Urea solubility test for Factor XIII and Clot retraction test. In all the three cases all of the above tests were within normal limits. Abnormal platelet aggregation was present in all 3 cases when induced by ADP, Epinephrine, Archidonic acid and Collagen. Reduced aggregation induced by archidonic acid and collagen was most sensitive and consistent in all the three cases. Aggregation induced by ADP showed normal primary wave but secondary wave of aggregation was markedly reduced during stimulation of PRP (Platelet rich plasma) by ADP or Epinephrine leading to detection of abnormal ADP release from the platelet. Platelet aggregation by ristocetin(both high and low concentration) was normal in all the cases. None of these cases showed parasitic infestation. In all the cases, the bruising or ecchymosis disappeared within 6 months and the abnormal platelet function returned to normal within 5 months. None of these cases had recurrence of these bleeding episodes.

Table 3: Review of cases with APDE from different countries.

Study	No. of cases with spontaneous bleed	No. of cases with eosinophilia (%)	M:F ratio	Platelet count	Platelet morphology	No of cases with parasitic infection (%)	Reporting country
Laosombat V et al. [9]	168	86	1.15:1	Normal	Abnormal	56	Thialand
Chin NS et al. [10]	31	7	NR	Normal	Abnormal	-	Malaysia
Ruiz-Saez et al. [11]	6	6	1:3	Normal	Abnormal	100	Venezuela
Wickramasinghe VP et al. [12]	14	14	3.6:1	Normal	Abnormal	100	Srilanka
S H Lim et al [13]	7	7		Normal	Abnormal	100	Singapore
M Ramanathan et al [14]	3	3	2:1	Normal	Abnormal	66	Singapore
G N Lucas et al. [15]	12	12	1.4:1	Normal	Abnormal	Nil	srilanka
Anselm chi wai lee et al [16]	1	1		Normal	Abnormal	Nil	Singapore
Ng Soo Chin et al [17]	31	7	6:1	Normal	Abnormal	Nil	Malaysia

DISCUSSION

In a study by Laosombatet al, [9] large number of cases with acquired platelet dysfunction with eosinophiliahad spontaneous bleeding manifestation including bruising on the extremities, body

and face off and on. All the children were in the age group of 13 months to 12.6 years with male to female ratio of 1.15:1. All these patient had normal number of platelets but the platelet morphology was abnormal in all the cases with eosinophilia. Similar findings were seen in this study also that, all the patient presented with spontaneous bleeding with normal number of platelet having abnormal morphology. In this review, we had all the 3 cases of age group between 11 months to 30 years and all of them were male. Most of the studies showed abnormal platelet aggregation induced by collagen, the most sensitive test in these patient. Also findings of aggretation study induced by ADP were abnormal, as reported by Laosombat et al, [9] Chin NS et al, [10] due to abnormal ADP release from the platelets detected in these patients by the absence of of secondary wave of aggregation during stimulation of platelet rich plasma by ADP or epinephrine. Similar results were seen in all the 3 cases in the present study. Also similar results were seen with regard to ristocetin induced platelet aggregation in this case study as it was reported by many researcher.

Many researchers have reported parasitic infestation in APDE (Acquired platelet dysfunction with eosinophilia) cases like study by Ruiz Saiz et al, [11] Wickramasinghe VP et al, [12] S H Lim et al, [13] in contrast, all the 3 cases in this study were extensively evaluated for evidence of parasitic infestation, but none have the positive findings.

The most striking feature was normal basic haemostatic screening test which comparises of bleeding time(BT), Clotting time(CT), Activated Partial Thromboplastin Time(APTT), Prothrombin time(PT), Factor XIII(Urea solubility test), and Clot retraction test. Only on the direct smear it was noticed that these patients have normal number of platelet with abnormal morphology and eosinophilia.

Majority of the patients with APDE had total serum IgE higher than 100 IU/ml. Many studies from Thailand have suggested that there is no definite correlation between serum IgE levels and eosinophilia. [9]

Majority of these patients with APDE do not receive any treatment except those who had severe bleeding symptoms, which is present in about 10% cases which require platelet concentrates to stop bleeding.

In patients with APDE, the spontaneous bleeding manifestation like ecchymosis and petichae disappear after 6 months of time without any treatment. It has been seen in the present study that after 4 months of regular follow up of these patients, the symptoms disappear as the eosinophilic counts in the peripheral blood drop. The abnormal morphology of platelets returns to normal in 4 months. It must be stressed in particular that any form of therapy has not been found useful in the treatment of these cases.

CONCLUSION

In conclusion, APDE is a worrisome benign, self limiting coagulopathy which lasts for 4-6 months time, and gets resolved without any treatment. The patients sometimes has to undergo various investigations with no concrete findings leaving the treating physician clueless. It is very important to recognize this benign condition (APDE) which clinically mimics Idiopathic Thrombocytopenic Purpura (ITP). All that is required is to reassure the patient and their parents and follow up closely.

REFERENCES

1. C. Transient, spontaneous Mitrakul bruising with long bleeding time and normal platelet count. Am J Clin Pathol 1975;68:81-6.

2. Suvatte V, Mahasandana C, Tanphaichitr V, Tuchinda S. Acquired platelet dysfunction with eosinophilia: Study of platelet function in 62 cases. Southeast Asian J Trop Med Pub Hlth 1979;10:358-67.
3. Isarangkura P, Hathirat P, Bintadish P, Lolekha S, Sasanakul W. Platelet morphology and immunologic study in acquired platelet dysfunction with eosinophilia (APDE). In:3rd Asian Congress of Pediatrics Bangkok, Thailand 1979:83.
4. Muthiah MM, Mitchell TR, Thorn CT. Acquired platelet dysfunction with eosinophilia. BMJ 1984;289:1044
5. Poon MC, Ng SC, Coppes MJ. Acquired platelet dysfunction with eosinophilia in white children. J Pediatr 1995;126:959-61.
6. Anselm Chi-wai Lee Children's Haematology and Cancer Centre, Mount Elizabeth Hospital, Singapore Unusual hematologic disease affecting Caucasian children traveling to Southeast Asia: acquired platelet dysfunction with eosinophilia. Hematology Reports 2012; volume 4:e5
7. Isarangkura P, Hathirat P. Common purpura in Thai children. Police Med J 1977;3:7-14.
8. Isarangkura P, Hathirat P, Bintadish P, Lolekha S, Sasanakul W. Platelet morphology and immunologic study in acquired platelet dysfunction with eosinophilia (APDE). In : 3rd Asian Congress of Pediatrics Bangkok, Thailand 1979:83.
9. Laosombat V, Wongchanchailert M, Sattayasevana B, Kietthubthew S, Wiriyasateinkul A.Acquired platelet dysfunction with eosinophilia in children in the south of Thailand. Platelets 2001 Feb;12(1):5-14.
10. Chin NS, Koong PLA study of 31 patients with easy bruising from University Hospital, Kuala Lumpur. Med J Malaysia. 1990 Dec;45(4):325-8.
11. Ruiz-Sáez A, Sifontes LN, Feijoo R, Certad G, Arenas-Pinto A, Pocaterra L, Ferrara G, Giménez R, Torres O, Goldstein C, Bosch NPlatelet dysfunction-eosinophilia syndrome in parasitized Venezuelan children. Am J of trop med hyg 2005 Aug;73(2):381-5
12. Wickramasinghe VP, Lamabadusuriya SP, Wijesundera MS. Ecchymoses: an unusual manifestation of toxocariasis in children. Ceylon medical journal 2001 Dec;46(4):130-1.
13. Lim SH, Tan CE, Agasthian T, Chew LS Acquired platelet dysfunction with eosinophilia: review of seven adult cases.J Clin Pathol. 1989 Sep;42(9):950-2
14. Ramanathan M, Duraisamy G. Acquired platelet dysfunction with eosinophilia (APDE): an under recognised condition. Med J Malaysia. 1987 Mar;42(1):53-5
15. Lucas GN, Seneviratne TR. A case of acquired platelet dysfunction with eosinophilia.Ceylon Med J. 1996 Sep;41(3):122.
16. Anselm Chi-wai Lee. Unusual hematologic disease affecting Caucasian children traveling to Southeast Asian acquired platelet dysfunction with eosinophilia:Hematology Reports 2012; volume 4:e5
17. Ng Soo Chin, PL Koong A study of 31 patients with easy bruising from University Hospital, Kuala Lumpur: Med. J. Malaysia Vol. 45 No. 4 December 1990.

How to cite this article: Singh BMK, Kurien A, Banerjee B et. al. Acquired platelet dysfunction with eosinophilia: a report of 3 cases with review of literature. Int J Health Sci Res. 2014;4(8):297-303.

****