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Case Report

Acquired Platelet Dysfunction with Eosinophilia: Report of Two Cases

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Abstract Acquired platelet dysfunction with eosinophilia (APDE) is an acquired bleeding disorder of unknown etiology characterized by bleeding, platelet dysfunction and eosinophilia. We reported two patients who presented with clinical features characteristic of APDE, and improved spontaneously without treatment.

Key words APDE; Eosinophilia; Platelet dysfunction

Introduction

Acquired platelet dysfunction with eosinophilia (APDE) is a benign, transient thrombocytopathy associated with significant eosinophilia and characterized by the sudden onset of bleeding tendency. Eosinophilia is found in most cases (83%),[1] but intestinal parasitic infestation, which should be the most common cause of eosinophilia, has been documented in only half of the affected children. The platelet dysfunction in these children is variable.[2] The disease usually resolves spontaneously within six to 12 months without specific treatment. In this first local report, we describe two patients managed by our unit in the past year.

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Case Reports

Case 1

A 4-year-old Caucasian boy presented with a 5-week history of spontaneous bruising associated with epistaxis. He traveled to Thailand five months ago. He was otherwise healthy except for skin allergy to dairy products and nuts in his infancy. There were no significant drug history including aspirin and no family history of bleeding disorders. Physical examination revealed multiple bruises and petechiae all over the body. No hepatosplenomegaly or lymphadenopathy was noted. Full blood count showed marked eosinophilia: haemoglobin (Hb) 12.5 g/dL, platelet count (Plt) $114x10^9$/L and white blood cell count (WBC) 12.7×10^9/L with 28% eosinophil (absolute eosinophil count 3.5×10^9/L, normal $<0.4 \times 10^9$/L). Thrombocytopenia was transient, and platelet count returned to normal about 20 days later. The clotting profile was normal. Prothromin time (PT) was 12.8 sec. (normal 11.3 to 13.2 sec.) and activated partial thromboplastin time (APTT) was 28 sec. (normal 27.6 to 37.6 sec.). Platelet function test showed only slight impairment in aggregation response to adrenaline with normal response to other agonists including ADP, ristocetin, arachidonic acid and collagen. Serum IgG and IgM were normal. Anti-nuclear factor was negative. Stool examination did not show any ova or parasite. No treatment was given. He continued to develop another crops of bruises despite normalization of platelet count. The bruises disappeared spontaneously about 1 month later. He still had mild eosinophilia (0.91×10^9/L) five months after presentation.

Case 2

An 8-year-old Nepalese girl presented with a 2-day history of multiple bruising and epistaxis. She had a history of congenital heart disease (ventricular septal defect with subpulmonary stenosis) and recurrent pneumonia since one month old. There was no family history of bleeding tendency and no significant drug history including aspirin. The girl was born in Nepal and the bruising occurred six months after she came to Hong Kong. Physical examination revealed multiple bruises on the face, chest and thigh. There was no heptosplenomegaly. Full blood count showed the following values: Hb: 12.0g/dl; PLT: 129 x 10^9/L (normal 150 to 400 x 10^9/L), WBC 22.25 x 10^9/L with 39% eosinophil (absolute eosinophil count: 8.86 x 10^9/L). PT (11.8 sec.) and APTT (31.6 sec.) were normal. Von Willebrand factor antigen was 0.68 iu/ml (normal 0.5 to 1.5 iu/ml) and ristocetin factor activity was 0.81 iu/ml (normal 0.5 to 1.5 iu/ml). Platelet function test showed a reduced aggregation response to collagen and adrenaline in amplitude, but normal response to ADP, ristocetin and arachidonic acid. Her serum IgE was increased. Anti-nuclear factor was negative. Stool examination failed to detect any ova and parasite. Her chest x-ray was normal. No specific treatment was given. About one month later, there was no significant fresh bruises noted and her platelet count returned to normal. However, the eosinophil was still elevated, ranging from two to four x10^9/L, even at six months after initial presentation.

Discussion

Acquired platelet dysfunction with eosinophilia (APDE) is an acquired bleeding disorder of unknown etiology associated with platelet dysfunction and eosinophilia. It is characterized by transient mild bleeding symptoms including ecchymoses, epistaxis, or gingival bleeding with variable platelet aggregation defects, and marked eosinophilia. This syndrome was first recognized as an acquired platelet dysfunction by Suvatte et al., (1974) and Mitrakul (1975). APDE was described mainly in indigenous Southeast Asian and East Indian children while rare cases of Caucasian children who developed easy bruising and eosinophilia after a visit to East or Southeast Asia have been reported.[3-4] It was previously thought to be unique to children, but a few adult cases had since been reported.[5] The mean age of onset was about 6.5 years.[4] The incidence of this syndrome is unknown. Both sexes are equally affected with the ratio of male: female being 1.4:1 and the same result has been confirmed by Mitrakul et al.[4-6]

The most common initial problem is painless ecchymoses, which may last from five days to one year. Approximately half of the children also have epistaxis and 8.1% patients suffer from severe bleeding. No central nervous system hemorrhages have been reported.[2] Bleeding problem typically disappears spontaneously within six to 12 months without specific treatment. Platelet transfusion may be useful in those patients with severe bleeding.[7] Once the syndrome resolved, recurrence is apparently rare.[3]

Platelet dysfunction that has been documented in 50% to 87% of the cases is probably due to the defect in platelet factor 3 release.[9] The platelet dysfunction in these children was variable, varying from mild abnormalities with subtle changes in clotting tests to very severe abnormalities demonstrable in all tests, including prolongation of the bleeding time, various abnormal patterns of platelet aggregation, and abnormal platelet factor 3 (PF3) release.[2] Platelet aggregation in response to stimulation by ADP, thrombin, and collagen is decreased, but the response to ristocetin is normal. The most sensitive test to detect abnormal platelet functions in this syndrome appeared to be platelet aggregation to collagen that was abnormal in 87.1% of the patients.[4] The abnormalities in APDE are different from those observed in patients taking aspirin or those with von Willebrand's disease. Aspirin ingestion can lead to abnormal platelet aggregation with ADP, collagen and arachidonic acid. In von Willebrand's disease, platelet agglutination with ristocetin is absent.

Eosinophilia was found in most cases (83%), varying from 3% to 69% of total WBC.[1] Intestinal parasitic infestation is the commonest apparent cause of eosinophilia, but it has been documented in only half of the affected children. The duration of symptoms and platelet dysfunction appeared unaffected by the rapidity of resolving eosinophilia following antihelminthic treatment.[2-8] The raised IgE concentration supports the contention that a type 1 IgE mediated reaction to either a parasite or other allergen is implicated in the pathogenesis of this condition.[5] Even though no parasite was detected in the stool, we still could not exclude that eosinophilia may be secondary to undiagnosed parasitic infestation in other sites, some of which may not be detected on routine stool examination. The reason why there is an association between the platelet dysfunction and eosinophilia, and the pathogenesis for bleeding tendency are still uncertain. It has been speculated that the high IgE in response to parasite causes mast cell degranulation and leads to in-vivo platelet activation.[1] This syndrome probably reflects an unusual immunological response to an inflammatory or infective process peculiar to Asian countries.[8]

APDE is a disease without confirmative diagnostic signs or test. We need to exclude other conditions before making the diagnosis. Immune thrombocytopenic purpura (ITP) should be included in the differential diagnosis. Both of

our cases had transient low platelet count, which returned to normal quickly. However, the bleeding tendency was out of proportion to platelet count and therefore ITP could not explain all the clinical and haematological features. The presence of thrombocytopenia does not rule out the diagnosis of APDE, as three percent of APDE patients showed mild transient thrombocytopenia in the previous reports.[1] Esosinophilia can be found in a number of causes including allergic disorders, parasitic infections, drug reactions or rarely be associated with some neoplastic or autoimmune disorders. From the clinical and investigatory results in our two patients, no definite cause of eosinophilia could be identified.

In summary, our two patients had bruises, eosinophilia and mild abnormality of platelet aggregation. They had no history of bleeding tendency. Both had traveled to other Asian countries. Their conditions improved spontaneously without specific treatment. The overall picture was consistent with APDE.

In conclusion, although APDE seems to be a rare disease entity locally, we need to be aware of this condition. High index of suspicion should be exercised in children with unexplained bruising associated with eosinophilia and a recent travelling history to Southeast Asian countries.

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