

## **Adverse Reaction of Topical Etofenamate: Petechial Eruption**

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### **ABSTRACT**

Etofenamate is a non-steroidal anti-inflammatory drug (NSAID). Clinical findings caused by etofenamate are uncommon. Allergic contact dermatitis is the most common cutaneous reaction reported. But petechial eruption due to etofenamate had not been reported yet. This report concerns an 11-year old male with petechial eruption after application of topical etofenamate.

Physicians need to be aware that patients can develop an asymptomatic purpuric eruption when etofenamate is ordered.

**Keywords:** Adverse reaction, etofenamate, petechial eruption

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## **INTRODUCTION**

Etofenamate is a non-steroidal anti-inflammatory drug (NSAID). It has analgesic, antirheumatic, antipyretic and anti-inflammatory properties. It is a non-selective COX (cyclo-oxygenase) inhibitor. Cyclo-oxygenase is an enzyme and is responsible for production of numerous chemicals, including prostaglandins in the body. Etofenamate inhibits prostaglandin synthesis, and provides analgesic and anti-inflammatory effects. After etofenamate, formulated in gel, is applied directly to inflamed tissue, it quickly penetrates through the corneal layer of the skin area of application and reaches therapeutically effective concentrations in the subcutis, fascias, ligaments and muscles. However, there are less systemic side effects of topical etofenamate (1, 2). Clinical adverse findings caused by etofenamate are uncommon. There have been infrequent reports on the incidence of side effects of etofenamate. Local skin irritation is observed [1 to 2%] (2). Contact sensitivity, allergic and photoallergic dermatitis are the most common cutaneous reactions reported (3–5). Petechial eruption due to etofenamate use was not documented (in PubMed) although vascular adverse reactions associated with NSAID use were reported. We report on an 11-year old male with petechial eruption after application of topical etofenamate.

## CASE REPORT

An 11-year old male was referred to our hospital because of petechial eruption in the chest, vomiting and fever. He was apparently well until one day previously. At that time, he had fever, vomiting and chest pain. Etofenamate (Rheumon<sup>®</sup>) gel (50 mg/gr) had been applied and massaged to the right chest about 12 hours before admission because of chest pain. About two hours after application, petechial eruption appeared in the exact site where etofenamate had been applied. He had not taken any other drug. History of signs and symptoms of systemic disease, drug allergies or atopy was not found.

On physical examination, he had tonsillopharyngitis and fever. There was typical palpable petechial eruption on the right chest area where etofenamate gel had been applied (Figure). Neurologic and cardiac examination results were normal.

Laboratory studies were performed and they were notable for a total white blood count of  $28.7 \times 10^9/L$  with neutrophilia (90%). A platelet count was within normal limits. Other routine haematologic tests were normal. C-reactive protein (CRP) level was 7.4 mg/dL (range:  $< 0.5$  mg/dL).

Oral penicillin treatment was ordered because of the high leucocyte count and positive CRP level for tonsillopharyngitis although cultures were negative. Within a few days, *Herpes labialis* appeared. The petechial lesions were asymptomatic and completely resolved without treatment in nine days.

## **DISCUSSION**

Etofenamate is an antranilic derivate with anti-inflammatory properties and it is usually administered topically (6). Despite its wide use, there are few cases presented by contact dermatitis (3–5, 6) and contact urticaria (7), suggesting a low allergenic potential. However, allergic vasculitis associated with celecoxib (a cyclooxygenase-2 selective NSAID) was reported in a few articles (8, 9). These reactions are generally related to systemic NSAID use. Here, we presented a child with petechial lesions due to topical etofenamate use. Petechial eruptions were not related to thrombocytopenia in our patient. All bleeding diathesis tests were normal. This adverse reaction was accepted as a local reaction. It may be related to a vasculitis, because the patient had no bleeding diathesis. Although the mechanism of this vascular reaction in topical drug use is not clear, a few mechanisms can be suggested for this patient. Etofenamate may trigger inhibition of endothelial prostacycline synthesis resulting in a prothrombotic state (10). Thus, it may provoke local extravasation of blood that may be facilitated by transient capillary fragility. On the other hand, it was also suggested that this was due to the local vasodilatation effect of topical etofenamate on the skin because topical etofenamate produces its anti-inflammatory action through prostaglandin synthesis inhibition. Dilatation of venules of the superficial plexus may cause mild oedema of the dermis and microthrombosis within some capillaries (11). Petechial lesions may be due to mechanical trauma. Mechanical trauma is a common cause of purpura in children, as previously reported in the literature (12, 13). It is known that skin and capillary fragility in infants is higher when compared to adults as demonstrated by the higher incidence of petechial eruptions after intense vomiting, coughing, or crying. Overdose of the drug might be a contributory factor in this case.

No previous references to this entity have been found for topical etofenamate. Physicians need to be aware that patients can develop an asymptomatic purpuric eruption,

which resolves without sequelae. We suggest that it must be used carefully in children with especially vasculitis syndromes and haemorrhagic diseases, since the clinical experience in these conditions in children is insufficient.

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Figure: Petechial eruption after application of etofenamate gel.