

Recurrent idiopathic angioedema in the presence of increased capillary fragility: an unusual case presentation

M. M. MILLER *U.T. Health Services Centre, Knoxville, Tennessee, U.S.A.*

(Received 18 June 1982; accepted for publication 4 August 1982)

Summary

A case of petechiae formation associated with recurrent idiopathic angioedema is presented. The mechanism for the petechial formation appears to be related to the underlying presence of increased capillary fragility in association with elevated venous pressure caused by angioedema. The persistence of the increased capillary fragility during the long, symptom-free intervals between acute episodes of angioedema suggests that the capillary fragility is unrelated to the pathologic process responsible for the angioedema.

Introduction

This report describes an unusual clinical presentation of acute recurrent idiopathic angioedema in a 7-year-old male child with persistent increased capillary fragility. He was initially hospitalized with a tentative diagnosis of Rocky Mountain spotted fever based upon the presence of petechiae associated with angioedema of the hands.

Materials and methods

This 7-year-old white male presented with a 3-year history of recurrent episodes of swelling of both hands with an associated petechial rash on the palms and dorsal aspects of the hands. During his initial episode in 1977, he was hospitalized by his pediatrician because of a sudden onset of hand swelling, and the presence of a petechial rash on his hands. The diagnosis of Rocky Mountain fever was suspected, but it was ruled out by a rapid resolution of symptoms and by the absence of a rise in complement fixation titers to *R. Rickettsii*. The swelling resolved in 2–3 days, and the petechial formation subsided in 4–5 days. Subsequent to this initial presentation, the patient has experienced approximately three such episodes each year. He has noticed some residual brown discoloration of the skin on the dorsal aspects of the hands which seemed to become progressively worse after each episode. His past medical history was unremarkable except for a history of recurrent bouts of serous otitis media.

On April 1, 1980, this patient was referred to us with bilateral angioedema of both hands and petechiae on the palms and dorsal aspects of the hands. Also noted at that

time was brown discoloration of the skin on the dorsal aspects of the hands. The mother stated that she had given the child aspirin 1 day prior to this episode, but she was certain aspirin ingestion had not occurred prior to the previous other episodes. The patient denied a personal history of excessive bleeding. No association was noted with exercise, pressure, sunlight, scratching, hot or cold water exposure, sweating, emotional upset, stress, food ingestion or other potential triggering factors of angioedema. The patient denied any fevers, chills, arthralgias, myalgias, night sweats, or weight loss. Previous symptoms otherwise were unremarkable except for occasional episodes of recurrent otitis media. There was no family history of urticaria, angioedema, or bleeding disorders.

Laboratory data at that time revealed a hematocrit of 36% and a white blood count of $11,100/\text{mm}^3$ with 85% polys and 15% lymphs. The platelet count was $227,000/\text{mm}^3$ and erythrocyte sedimentation rate was 6 mm/h. Complement studies revealed C_3 -235 mg% (88–194% normal), and C_4 -22 mg% (16–53% normal).

The patient was advised to avoid all aspirin products and a retrospective food and drug diary was initiated. Symptomatic treatment included hydroxyzine 25 mg. Q.I.D., ephedrine sulfate 25 mg. Q.I.D., and prednisone 40 mg. Q.D. $\times$ 5 days. Five days later the swelling had dissipated and the petechiae had become ecchymotic but were resolving.

Five weeks later while the patient was asymptomatic and on no medications, a Rumpel-Leede test produced generalized numerous petechiae of the arm. No aspirin products or other drugs capable of interfering with platelet aggregation had been taken during the month preceeding the Rumpel-Leede test. Results of coagulation studies at this time included: Ivy bleeding time 8 min (normal 1–7 minutes); platelet count $133,000/\text{mm}^3$ (normal 150,000–400,000); Lee-White clotting time 9 min (normal 9–17 minutes); clot retraction beginning at 1 h and complete by 24 h. Platelet aggregation studies using ristocetin, collagen, ADP, and epinephrine were 66%, 54%, 48%, and 0% of the predicted normal respectively. A mecholyl intradermal skin test and cholinergic exercise test was negative.

Immersion of his foot in a 110°F water bath failed to produce swelling or petechiae. The patient was followed for 6 months and had two short episodes of the angioedema and petechial formation lasting several days. No known triggering factors could be identified.

In December 1980, after the patient had remained asymptomatic for 5 months and was taking no medications, a repeat Rumpel-Leede test remained positive. The patient had no laboratory evidence of hypertension, diabetes, or chronic renal disease. At this time, a haematology consultation was obtained and the coagulation studies were repeated. The Ivy bleeding time was 6 min. The platelet count was $235,000/\text{mm}^3$, the prothrombin time and partial thromboplastin time were normal. The clot retraction began at $\frac{1}{2}$ h and was complete by 2 h. A Factor-VIII level was 114% activity (normals 50–170%). Qualitative platelet aggregation studies at this time with ristocetin, epinephrine, collagen, and ADP were 81%, 80%, 68%, and 80% of the predicted normal respectively. These studies showed improvement from the previous aggregation studies done in June 1980. Rumpel-Leede tests performed on the patient's mother and three siblings were negative. His father is deceased.

The haematology consultation indicated that the qualitative platelet abnormalities originally noted were not of sufficient magnitude to produce the massive petechial formation during the Rumpel-Leede test. The persistently positive Rumpel-Leede test,

even when the qualitative platelet studies were normal, also suggests that the cause of the petechial formation is capillary fragility, not thrombocytopathy. The absence of capillary fragility in his siblings and mother suggests that his capillary fragility is not familial.

In conclusion, the petechial formation during the Rumpel-Leede test in this patient suggests the presence of increased capillary fragility. The etiology of this capillary fragility appears to be idiopathic since chronic renal disease, diabetes mellitus, and hypertension and familial causes were not found (Wintrobe, 1967).

Discussion

This patient's unusual presentation of recurrent acute idiopathic angioedema of the hands appears to be related to the concomitant presence of persistent increased capillary fragility in this patient. The mild qualitative platelet defect and the minimal prolonged Ivy bleeding time found initially, while the patient was asymptomatic, do not appear to be of sufficient magnitude to account for the tremendous amount of petechial and ecchymotic formation noted during the Rumpel-Leede test and the episodes of angioedema. Additionally, the Rumpel-Leede test remained positive 6 months later during a time when the patient was asymptomatic and his platelet aggregation and Ivy bleeding time were normal. This suggests that the petechial formation noted during the bouts of angioedema is a result of persistent, underlying capillary fragility unrelated to the unidentified triggering mechanisms responsible for the recurrent idiopathic angioedema in this patient. The normal sedimentation rate and lack of hypocomplementemia during acute episodes tend to rule out circulatory immune complexes as a cause for the increased capillary fragility. Failure to identify a cause of capillary fragility in this patient would suggest that this patient has idiopathic capillary fragility, which occurs in approximately 8% of the population (Kramer, 1961).

A plausible explanation for this unique presentation of intermittent petechiae is that the recurrent, idiopathic angioedema produces compression of the veins and increases venous pressure locally, thus producing an *in-vivo* Rumpel-Leede test. The idiopathic increased capillary fragility in this patient is responsible for the petechiae formation which occurs whenever the venous pressures are significantly elevated by local venous compression from the idiopathic angioedema.

In conclusion, this patient appears to have recurrent acute idiopathic angioedema and unrelated chronic idiopathic capillary fragility. The combination of these two disorders is manifested by petechial formation in association with the acute episodes of idiopathic angioedema.

References

- KRAMAR, J. (1961) Capillary resistance and its relation to bleeding. In: *Blood Platelets* (eds S. A. Johnson, R. W. Monto, J. W. Rubeck & R. C. Horn) Little & Brown, Boston.
- WINTROBE, M.M. (ed.) (1967) *Clinical Hematology*, p. 325. Lea & Febiger Co., Philadelphia.

This document is a scanned copy of a printed document. No warranty is given about the accuracy of the copy. Users should refer to the original published version of the material.