Comments on 'Validity and responsiveness of the Osnabrück Hand Eczema Severity Index (OHSI): a methodological study': reply from authors

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SIR, Thank you for the opportunity to respond to the letter of Apfelbacher and Hankins on our article 'Validity and responsiveness of the Osnabrück Hand Eczema Severity Index (OHSI): a methodological study'.[1]

In their letter, the authors emphasize the importance of validation studies for instruments that assess the severity and change in hand dermatitis. We are pleased by the authors' support and appreciate any suggestion that might improve our work or the work of any other research group facing the obstacles of a validation study.

Besides the Manuscore,[2] there are other instruments available that could be used as 'gold standards'. All instruments mentioned in the letter were already mentioned in our study. Neither of the other two instruments is validated to such an extent that it presents itself as the choice *sine qua non* as 'gold standard'. As we described in our paper, we used the Manuscore for practical reasons. The main focus of our validation study was responsiveness to change. Therefore the Hand Eczema Severity Index[3] and the photographic guide[4] had no advantage over the Manuscore – as none of the three instruments has so far been validated in a longitudinal study for responsiveness to change.

To measure responsiveness to change we compared changes in the scores after treatment between the two measurement instruments by using effect sizes. We stated that the effect sizes pre- to post-treatment were not different between the Manuscore and the OHSI scoring and showed similar clinically meaningful improvements in the OHSI scores over 1 year. Because of space restrictions we had omitted the following Table (Table 1). Ninety per cent of the patients with improved results based on Manuscore scoring also exhibited improved results in the OHSI. Unchanged and worsened results were so scarce based on the Manuscore scoring that no meaningful conclusion for the comparison between the two instruments can be drawn.

Table 1 Overall changes of hand eczema rated by the Manuscore and Osnabrück Hand Eczema Severity Index (OHSI) after repeated measurement: numbers of patients

	Manuscore			
	Improved	Unchanged	Worsened	Total
OHSI				
Improved	53	1	1	55
Unchanged	5	0	0	5
Worsened	1	1	0	2
Total	59	2	1	62

We conclude our paper with the sentence: 'To affirm the validity of the OHSI a larger cohort is needed'. An additional conclusion – as recommended by the letter of Apfelbacher and Hankins – is: 'As a gold standard other scores should be considered in further studies'.

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Key words: *responsiveness, validity*

Conflicts of interest: none declared.

Romiplostim-induced erythromelalgia in a patient with idiopathic thrombocytopenic purpura

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SIR, Erythromelalgia is a rare condition characterized by recurrent disabling episodes of hot, red and painful distal extremities.[1] We report here a case induced by romiplostim, a thrombopoietin agonist, in a patient with idiopathic thrombocytopenic purpura.

A 59-year-old man was referred in our department for acute paroxysmal pain of the distal extremities, relieved by cooling in cold water. His personal medical data were notable for an 18-year history of idiopathic thrombocytopenic purpura (ITP). He was initially treated by splenectomy, followed by corticosteroids and, more recently, rituximab. A recent flare with a decrease in the platelet count prompted the initiation of treatment by subcutaneous injection of romiplostim, a thrombopoiesis-stimulating protein, at a dose of 2 $\mu g\ kg^{-1}$.

The platelet count was 34×10^9 L^{-1} at the time of injection. Within 48 h, the patient developed progressive, sleep-disturbing, burning pain in the hands and feet. Symptoms were relieved only by immersion of the extremities in cold water. Physical examination revealed hot, red, intensely painful erythema of the fingers and toes without a lack of arterial pulse (Fig. 1). The blood cell count disclosed a rapid increase in the platelet count from 98×10^9 to 213×10^9 L^{-1} at, respectively, days 3 and 5 postinjection. Microscopic examination of a punch skin biopsy revealed intravascular microthrombi in the mid and deep dermis (Fig. 2). Laboratory tests, including antinuclear, antidouble stranded DNA, antiextractable nuclear antigen, antiphospholipid and anticardiolipin antibodies, complement levels (C3, C4 and CH50), cryoglobulinaemia, cryofibrinogenaemia and cold agglutinins, were negative. Arterial ultrasound imaging of the lower limbs was normal. Lysine acetylsalicylate (160 mg daily, Kardegic®; Sanofi-Aventis, Paris, France) and cessation of romiplostim treatment provided relief within a few days. Romiplostim was reintroduced 1 month later at a dose of 1 μg kg^{-1} weekly. A relapse of erythromelalgia was observed within 48 h of each injection with an improvement before the next injection.

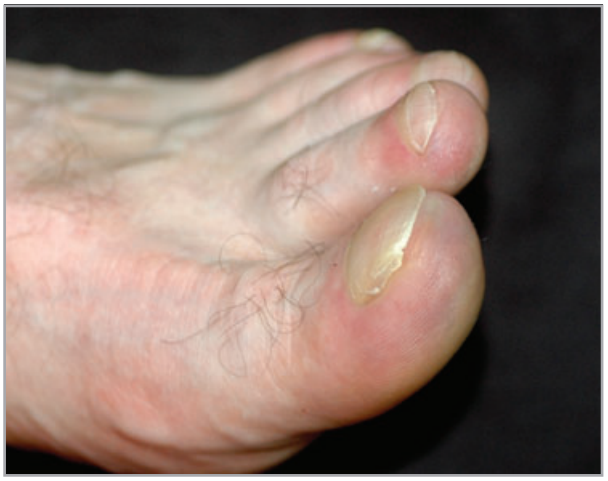

Fig 1. Painful erythema of the feet under romiplostim.

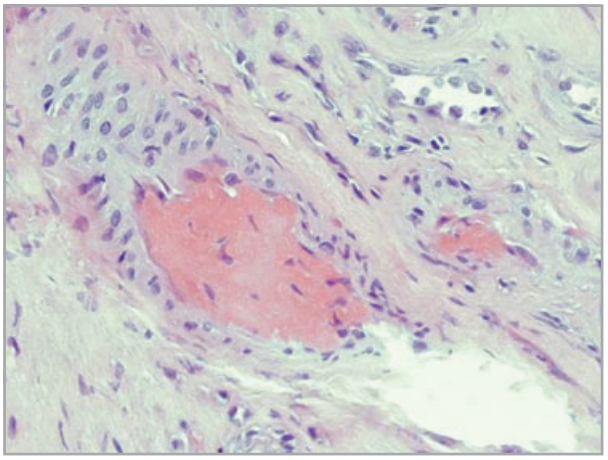

Fig 2. Thrombosis in the dermis (haematoxylin and eosin stain).

We report here the first case of erythromelalgia induced by romiplostim in a patient with ITP. Observations that support a relationship between romiplostim and erythromelalgia include: (i) no episodes prior to treatment initiation, (ii) onset 48 h after the subcutaneous injection, (iii) clinical improvement after drug withdrawal and (iv) relapse after each drug injection within a similar timeframe.

Erythromelalgia is a rare condition characterized by recurrent episodes of intensely painful and disabling erythema of the distal extremities. Secondary forms are usually associated with haematological disorders such as myeloproliferative syndromes, as well as connective tissue disorders, neurological disorders and various other conditions.[1] Erythromelalgia was previously reported in a patient with ITP.[2] However, the episodes were related to concomitant decreases in platelet count. As soon as the ITP was controlled and the platelet count returned to normal, the erythromelalgia cleared. In our case, the patient had an 18-year history of ITP with no episodes of erythromelalgia and the present symptoms were not related to a drop in platelet count.

There are several reports of drug-induced erythromelalgia, especially with calcium channel blockers and bromocriptine.[1] Romiplostim (developed under the name AMG 531) is a subcutaneously administered thrombopoietin receptor agonist currently being studied for the management of ITP.[3–5] Romiplostim stimulates platelet production and counts without inducing neutralizing antibodies.[4] In clinical trials, side-effects have usually been mild and related to ITP.[3–5] To the best of our knowledge, no case of erythromelalgia has ever been reported. However, in a recent study,[5] 13% of the treated patients presented 'pain in extremity' vs. 5% in the placebo group, with no further details given. The authors concluded that the small sample size did not allow any conclusions to be drawn. Moreover, two cases of arterial thromboembolic events were reported in patients with prior cardiovascular history.[5] Platelet counts increased in both patients above their usual baseline but remained within the normal range.[5] In our case, the erythromelalgia occurred concomitantly with the sudden increase in platelet count induced by romiplostim. Histology confirmed a thrombotic event within the small cutaneous blood vessels. As stated by Kuter *et al.*,[5] romiplostim does not directly increase platelet activation but there is a known linear increase in platelet deposition with an increase in platelet count after treatment with recombinant thrombopoietin.

We report the first case of erythromelalgia induced by increased platelet count after romiplostim injection. The respective roles of the romiplostim injection and increased platelet count in the reported case remain to be determined.

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Key words: *adverse effect, drug induced, erythromelalgia, idiopathic thrombocytopenic purpura, romiplostim*

Conflicts of interest: none declared.

Overweight and childhood psoriasis

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SIR, A few studies conducted in adults have found a positive association between being overweight and risk of psoriasis, a serious disease affecting approximately 2% of the population. The relative risk was 1·5–2 for overweight and obese individuals.[1,2]

The incidence of childhood psoriasis is unknown,[3] but it has been reported that 10% of all cases occurred before the age of 10 years and 2% at < 2 years of age.[4] If the association between overweight and psoriasis is present also in children, the increasing incidence of childhood obesity may be an emerging public health issue. In Italy the prevalence of overweight in preschool children was estimated to be 4·4%[5] while in adolescents (aged 10–16 years) it was 14·9%.[6] We have therefore conducted a case–control study between January and December 2005, at the Division of Pediatric Dermatology of San Paolo Hospital, Milan, Italy, which treats children under the age of 15 years. Cases were children with a first diagnosis of psoriasis made by a dermatologist.

All eligible patients seen consecutively during the study period were invited to participate and all were included. We excluded children with eczema–psoriasis overlap and/or with a family history of both atopic dermatitis and psoriasis. All participants' parents gave written informed consent.

In accordance with the International Psoriasis Council,[7] cases were classified as napkin psoriasis (n = 4), psoriasis localized to the scalp (n = 8), plaque psoriasis (n = 68), guttate psoriasis (n = 10) and nail psoriasis (n = 6). Diagnoses in the control group included atopic dermatitis (n = 53), angiomas and vascular malformations (n = 6), viral diseases (n = 11), bacterial diseases (n = 3), fungal diseases (n = 3), acne (n = 3), naevi (n = 5), pityriasis rosea (n = 2), pityriasis alba (n = 4), parasitic diseases (n = 5) and alopecia areata (n = 5). Thus 96 cases (52 boys and 44 girls) and 100 controls (43 boys and 57 girls) were included.

Using a structured questionnaire, we collected information on height, weight, dietary habits of the child, family history of psoriasis (FHP), and smoking habits and alcohol consumption of the mother. We calculated a percentage measure of body mass index (BMI) as the actual weight of the child divided by the 50th centile weight at the age when the child's height was on the 50th centile. Values over 110% were considered overweight, 90–110% normal weight, and below 90% underweight.[8]

Odds ratios (ORs), as estimators of the relative risk, and the corresponding 95% confidence intervals (CIs) were computed using unconditional multiple logistic regression with maximum likelihood fitting, in order to take into account the effect of age, sex and FHP.

The mean ± SD age was 8·7 ± 2·9 years in cases and 7·3 ± 3·5 years in controls. FHP in first- or second-degree relatives was reported by 55·2% of cases and 10% of controls.

Table 1 gives the distribution of cases and controls according to BMI. A positive association between overweight and psoriasis was found (OR 2·55, 95% CI 1·31–4·96) when adjusted for sex and age. Similar results were evident after adjustment for sex, age and FHP (OR 3·38, 95% CI 1·56–7·30). The multivariate OR was 1·52 (95% CI 0·60–3·89) for underweight children.

Table 2 considers the association between measures of body weight and psoriasis in strata of sex and age. None of the stratification variables showed a significant interaction with BMI. Significant positive associations were found for overweight in boys (OR 4·63, 95% CI 1·40–15·28) and younger children (age ≤ 10 years) (OR 3·19, 95% CI 1·40–7·28).

Some limitations of this study should be considered. Cases were recruited regardless of disease severity and more