Reviewer's report

Title: Successful negative pressure wound therapy for necrotizing fasciitis in a child with cyclic neutropenia

Version: 1 Date: 4 September 2014

Reviewer: Michael Hawkes

Reviewer's report:

The authors are to be congratulated on an interesting case report where a molecular diagnosis of ELANE leukocyte elastase mutation was associated with cyclic neutropenia, the likely predisposing factor for an aggressive soft tissue infection and Pseudomonas aeruginosa bacteremia.

The major strength of the report is the molecular diagnosis, and description of a new point mutation in the ELANE gene, present in both mother and daughter with similar neutropenia phenotype (autosomal dominant inheritance).

(Discretionary revision)
I am less impressed with the "wound vac" aspect of the case, which may have accelerated healing, or may have been only temporally associated with the healing expected with surgical debridement and (presumably) appropriate antibiotic therapy. This anecdotal report cannot establish with any certainty the benefit of negative pressure dressings in the management of necrotising fasciitis. I wonder if this aspect should be given less importance in the case report (do not include it in the title).

(Discretionary revision)
The authors consistently use the term necrotizing fasciitis throughout the text which is probably an accurate pathologic description (but cellulitis and myositis also seem to be present). The microbiology is a bit different from the usual pattern of nec fasc (usually pure culture of group A strep, or polymicrobial necrotising gangrene with anaerobes). The initial lesion (knowing the microbiological etiology) is reminiscent of "ecthyma gangrenosum". "Deep soft tissue infection" might be another less leading description of the infection (rather than nec fasc).

Where did the Pseudomonas come from? We generally think of this as a nosocomial pathogen - it would seem there was a history of recurrent hospitalizations for pneumonia. Comment on the microbiology in the discussion would be helpful.

(Minor essential revisions)
1. Please report the antibiotic susceptibility pattern of the Pseudomonas isolate and the antibiotics used to treat the deep soft tissue infection and bacteremia.
2. Please provide the method used for species-level identification of the (coagulase-negative) Staphylococcus hominis, antibiotic susceptibility and whether the authors considered this a causative pathogen or a skin commensal.

3. ELANE mutations are thought to lead to a "gain-of-function" in the neutrophil granule protein leukocyte elastase (aberrant processing, packaging), with consequent cellular toxicity to neutrophil precursors. The point mutation (c.373G>T, p.Gly125Trp) in exon 4 appeared to confer "deteriorating protein function" according to an in silico analysis that was not well described. Can the authors more clearly relate the mutation (seen in both mother and daughter with similar CN phenotype) to the protein structure and speculate on the basis of the neutropenia? E.g., missense mutation in the terminal peptide that confers protection to cellular elements during protein synthesis, or other. I think it would be valuable to add this newly described point mutation to a database such as the Human Gene Mutation Database.

4. Please provide the serial neutrophil counts in hospital that demonstrated the cyclic pattern of the neutropenia. Providing detail for this component of the phenotype will be convincing for CN (rather than an incompletely documented, suspected CN). The phenotype should be well described for a clear association with the genetic mutation in ELANE gene.

(Minor essential revisions)

Editorial remarks:

"very rare", "extremely rare" are used throughout the text for conditions that we do see from time to time in clinical practice. I think "rare" suffices

CN appears in abstract without prior definition of the abbreviation

fasciitis "on" the axilla - wording awkward - fasciitis of the axillary tissues...?

bottom of page 2: suspicion of congenital neutropenia

"under the diagnosis" (p3) awkward

p5: angiogenesis

other awkward sentences: have another native English speaker read through for grammar/sentence structure

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Needs some language corrections before being published

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
I declare that I have no competing interests