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Non-Hodgkin's lymphoma in a patient with leucocyte adhesion deficiency

To the Editor,

Leucocyte adhesion deficiency type 1 (LAD-1) is a rare autosomal recessive primary immunodeficiency disorder, characterised by the absence or deficient expression of the adhesion molecules on leucocytes. The disease is usually associated with leucocytosis, recurrent severe bacterial and fungal infections without pus formation and impaired wound healing. Omphalitis, delayed umbilical cord separation, perirectal abscess, sepsis, necrotising enterocolitis, pneumonia, gingivitis and periodontitis are common features of disease.[1–3] Although some forms of primary immunodeficiency diseases could develop malignancies, there is no report of non-Hodgkin's lymphoma in patients with LAD.

Herein a boy is presented who was admitted to the NICU ward because of omphalitis, sepsis, icterus and erythematus rashes. He was the second child of consanguineous parents. The first child of the family was a girl who died at three months of age due to pneumonia. The culture of umbilical discharge of the patient was *Pseudomonas* spp. While he was receiving treatment, he developed right foot cellulites. Radioisotope scanning showed arthritis in right knee. His umbilical cord had been cut on 32 days of life. Lab data revealed leucocytosis 30,000/mm^3 with neutrophilia (65%) and eosinophilia (10%). Serum immunoglobulin (Ig)G, IgM, IgA, and NBT tests were all normal. Peripheral blood flow cytometric analysis revealed normal T-, B- and NK cell numbers, but was compatible with LAD-1 (CD18 = 0.5%, CD11a = 0.5%, CD11b = 0%, CD11c = 1.2%). He had history of several episodes of sepsis, pneumonia, diarrhoea, typhlitis, necrotic skin ulcers and infections because of *Pseudomonas* spp. and *S. aureus* after diagnosis.

The 3rd sibling of this family is a girl, who was admitted to the NICU at age of 30 days because of delayed separation of umbilical cord and omphalitis. Her laboratory data revealed leucocytosis (27,000/mm^3) with neutrophilia (82%). Serum immunoglobulins and NBT were normal. Chemotaxis was impaired and peripheral blood flow cytometric analysis revealed low expression of CD18 (CD18 = 1.6%, CD11a = 0.2%, CD11b = 1.0%, CD11c = 5%). T-, B- and NK subpopulation numbers were normal. Now, she is six years old and has undergone recurrent severe diarrhoea, pneumonia, skin infections with necrotic ulcers due to *Pseudomonas* spp. and *S. aureus*, chronic gingivitis and chronic otitis media with discharge. Both siblings have failure to thrive.

During follow-up, the boy was admitted into the hospital due to abdominal mass at the age of seven years. The mass (3 cm × 4 cm) removed in appendix with partial residue in ileocecal region during laparotomy. Pathology reported diffuse large B-cell lymphoma as a primary tumour in the abdomen being positive for CD20 and CD22. Genetic evaluation showed *t* (8:14) in mass. Other investigation to determine the clinical extent of the disease for staging showed stage II of disease. He received LMB-96 protocol. During chemotherapy, he had several episodes of severe infection and abscess formation. The result of treatment was excellent after treatment and now he is alive, 11 years old, without any recurrence of disease.

Several manifestations have been reported in LAD patients, the severity of which appears to be related to the degree of surface expression of CD18 and CD11. However, to the best of our knowledge, NHL has not been reported in LAD. However, unfortunately, the lymphoma itself was not tested for CD11 or CD18. NHL, which is malignant proliferation of lymphocytes, seems to be one of the most common childhood malignancies. As genetic abnormalities are risk factors for NHL, such abnormalities in integrin molecules could predispose patients to malignancy in lower ages. As β2 integrins are essential for the regulation of antigen-dependent activation threshold, low expression of the molecule could cause deficiency in the quantitative and qualitative of CD4+ T-cells and lymphocytes that normally regulate immune function and suppress malignant clone. There is some evidence showing association of primary immunodeficiency disorders and cancers.[4] Although predisposition to viral infections as well as susceptibility to DNA breakage were considered as specific aetiologies of a number of cancers in certain immunodeficiencies, the exact biological pathway and mechanisms for such association have not been completely recognised. Development of malignancy in LAD patients could provide insight into the possible role of β2 integrins in cancers.

Ethical disclosures

Protection of human subjects and animals in research. Protection of human and animal subjects. The authors declare that the procedures followed were in accordance with the regulations of the responsible Clinical Research Ethics Committee and in accordance with those of the World Medical Association and the Helsinki Declaration.

Patients' data protection. Confidentiality of data. The authors declare that they have followed the protocols of their work centre on the publication of patient data and that all the patients included in the study have received sufficient information and have given their informed consent in writing to participate in that study.

Right to privacy and informed consent. Right to privacy and informed consent. The authors have obtained the informed consent of the patients and/or subjects mentioned in the article. The author for correspondence is in possession of this document.

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Separation of the four most important latex allergens from latex gloves: A potential tool for diagnosis and immunotherapy purposes

To the Editor,

Due to a more wide-spread use of latex products, in particular medical gloves, allergy to natural rubber latex (NRL) had posed serious concerns during the 1980s and 90s. Currently, it is known that this epidemic of allergic reactions is especially prevalent in certain occupational groups repeatedly exposed to latex products, such as health care workers (HCW) and patients with spina bifida (SBP).[1]

The identification of the patients who become sensitised and are likely to suffer from symptoms upon repeated exposure to latex products is a major goal for prevention of the allergic reactions. It is generally accepted that the diagnosis must be based on the clinical history and on a confirmative assay which may include *in vivo* tests such as skin prick tests (SPT), provocation tests and/or laboratory-based *in vitro* analyses.[2] Among these, SPT are described as the most reliable *in vivo* method for diagnosis of sensitisation to latex proteins.[3] However, a potential low diagnostic sensitivity of latex SPT is associated to poorly represented and/or denatured allergens, such as Hev b 3 and Hev b 5.[4,5] In fact, to perform an appropriate diagnosis, it is critical that the applied extract contains an adequate amount of all clinically relevant allergen components.[4]