profesionales/saludPublica/ccayes/alertasActual/alertaMonkeypox.
2. Eltvedt AK, Christiansen M, Poulsen A. A case report of Monkeypox in a 4-year-old boy from the DR Congo: challenges of diagnosis and management. Case Rep Pediatr. 2020;2020:8572596, http://dx.doi.org/10.1155/2020/8572596.
3. Adler H, Gould S, Hine P, Snell LB, Wong W, Houlihan CF, et al. Clinical features and management of human monkeypox: a retrospective observational study in the UK. Lancet Infect Dis. 2022;22:1153–62, http://dx.doi.org/10.1016/S1473-3099(22)00228-6.
4. Rodríguez-Cuadrado F, Pinto-Pulido E, Fernández-Parrado M. Inmunoglobulina anti-*Vaccinia* y profilaxis postexposición mediante vacuna basada en *Vaccinia* para el control del brote de viruela símica (*Monkeypox*). Actas Dermosifiliogr. 2022, http://dx.doi.org/10.1016/j.ad.2022.08.017. In press.

Marc Roguera Sopena*, Laura Naqui Xicota,
Águeda Hernández Rodríguez,
María Jesús Méndez Hernández,
Carlos Rodrigo Gonzalo de Liria

Hospital Germans Trias i Pujol, Badalona, Barcelona, Spain

* Corresponding author.
E-mail address: mroguera.germanstrias@gencat.cat
(M. Roguera Sopena).

https://doi.org/10.1016/j.anpede.2022.10.003

Necrotizing enterocolitis after intravenous immunoglobulin administration and exchange transfusion in a newborn with hemolytic disease due to anti-c☆

Enterocolitis necrotizante tras administración de inmunoglobulinas y exanguinotransfusión en anemia hemolítica por anti-c

Dear Editor:

Haemolytic disease of the foetus and newborn (HDFN) affects 3–80 per 100 000 patients each year. Although the most frequent cause of HDFN is Rhesus D (RhD) antigen alloimmunization, other red blood cell antigens can cause the disease, for instance, through anti-c isoimmunization. When the incompatibility is severe, it can cause foetal anaemia, hydrops fetalis and even intrauterine death. In neonates, phototherapy is the most widely used treatment in mild and moderate cases. In severe cases, intravenous immunoglobulin (IVIG) and exchange transfusion may be useful to prevent bilirubin encephalopathy.[1]

We present the case of a preterm newborn with HDFN caused by an uncommon type of antibodies (anti-c). The patient experienced an insidious course that required treatment with IVIG and exchange transfusion. She then developed necrotising enterocolitis (NEC).

The patient was a newborn girl admitted to our hospital due to jaundice with onset within 24 h of birth. She was the second child of a healthy mother aged 37 years that had received a diagnosis at 24 weeks of gestation of Rh isoimmunization due to anti-c antibodies. Foetal ultrasound examinations were carried out, which did not detect abnormalities in the foetus, with the exception of mild anaemia at 30 weeks of gestation.

The patient was born at 35^{+1} weeks of gestation. Her blood type was A Rh+ and the direct Coombs tests was positive, evincing the presence of anti-c antibodies. At 24 h post birth, the physical examination of the patient was normal with the exception of jaundice. Laboratory tests confirmed hyperbilirubinaemia (total bilirubin, 13.5 mg/dL; normal range, <8 mg/dL) in the absence of anaemia (haemoglobin, 16.7 g/dL), leading to initiation of intensive phototherapy for 14 days with a positive outcome. Bilirubin levels remained below the exchange range. Other tests were performed to rule out alternative diagnoses to hyperbilirubinaemia.

At 14 days post birth, the patient developed anaemia (haemoglobin, 7.7 g/dL; normal range, 12.5–20.5), leading to administration of IVIG (1 g/kg IV over 6 h). The patient remained haemodynamically stable before and during treatment. The anaemia progressed despite IVIG (haemoglobin, 6.7 g/dL 12 h after immunoglobulin administration), so the patient underwent partial exchange transfusion (80 cc/kg) delivered through a central venous catheter (left femoral vein). There were no adverse events associated with the transfusion. The haemoglobin concentration increased to 12.3 g/dL (Fig. 1). A few hours after the transfusion was completed, the patient exhibited general deterioration with abdominal distension and bilious vomiting. She required endotracheal intubation and haemodynamic support with dopamine. The findings of the abdominal radiograph were suggestive of NEC (Fig. 2). The patient underwent an urgent laparotomy that confirmed the diagnosis. This was followed by performance of an end ileostomy with removal of the distal ileum and ascending colon. After the surgery, the patient recovered gradually and was discharged at day 30.

Minor blood group incompatibility has been found to be responsible for 3%–5% of cases of haemolytic jaundice in neonates.[2] Antigen c is one of the most immunogenic antigens, following antigen D, with immunization usually developing antenatally and associated with a risk of moderate to severe HDFN.[3]

Haemolytic disease of the foetus and newborn can cause sustained anaemia, possibly with antenatal onset, causing tissue hypoperfusion and particularly affecting the gastroin-

☆ Previous presentation: This study was presented at the XXVIII Congress of the Sociedad Española de Neonatología in October 2021with the title ''Enterocolitis necrotizante tras la administración de inmunoglobulina intravenosa y transfusión de hematíes en pretérmino tardío con enfermedad hemolítica anti-c''.

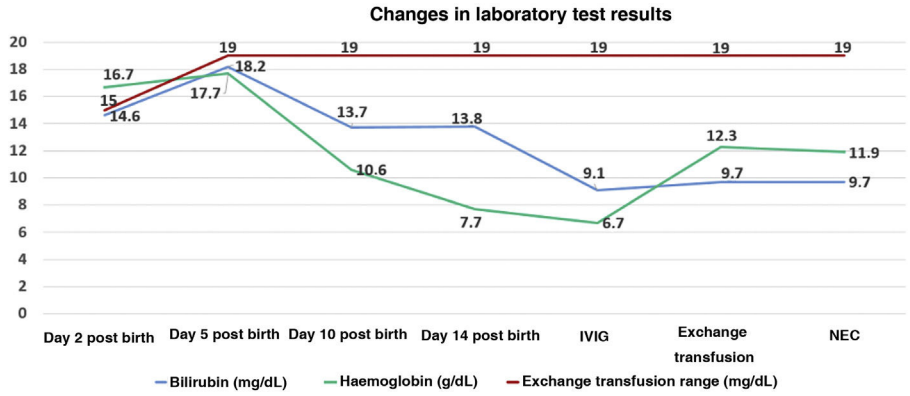

Figure 1 Changes in laboratory test results.

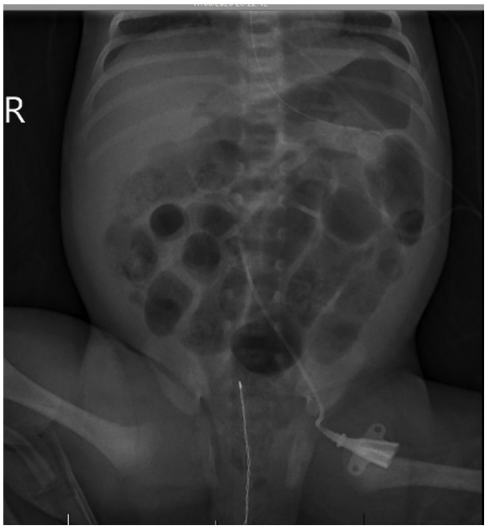

Figure 2 Abdominal radiograph.

testinal tract.[4] In addition, it is associated with an increased risk of preterm birth, and enterocolitis is more frequent in preterm newborns.

Administration of immunoglobulin is recommended for treatment of hyperbilirubinaemia refractory to phototherapy and also of anaemia secondary to HDFN. Intravenous immunoglobulin also seems to be associated with the development of NEC, as it causes an increase in blood viscosity that may give rise to the formation of microthrombi and a reduced mesenteric blood flow. Figueras-Aloy et al. described the association between the administration of immunoglobulin with haemolytic disease and the development of NEC.[5]

The association between the administration of blood products and NEC is also well established, with NEC usually appearing between 24 and 48 h post transfusion.[6] The factors that promote enterocolitis are inflammation secondary to the infusion of red blood cells, the decreased capacity of haemoglobin in banked red blood cells to delivery oxygen compared to foetal haemoglobin and the increased viscosity of the blood.

Haemolytic disease of the foetus and newborn, IVIG therapy and exchange transfusion are independently associated with the development of NEC. In our patient, anaemia became severe from 14 days post birth, although it is not possible to determine whether earlier administration of IVIG or exchange transfusion could have prevented NEC. At any rate, based on the sequence of events, IVIG administration seems the most plausible explanation for NEC, as necrosis was already present at the time of surgery, indicating that ischaemia had started at least 12 h before the operation.

In conclusion, neonates with HDFN are at increased risk of requiring IVIG and exchange transfusion, both associated with the development of NEC, and therefore require careful monitoring.

Funding

This research did not receive any external funding.

References

1. Delaney M, Matthews DC. Hemolytic disease of the fetus and newborn: managing themother, fetus, and newborn. Hematology Am Soc Hematol Educ Program. 2015;2015:146–51.
2. Gökçe İK, Güzoğlu N, Öncel MY, Çalişici E, Canpolat FE, Dilmen U. A hemolytic disease due to minor blood group (Anti-C and Anti-E) incompatibility leading to symptomatic anemia in the neonatal period. Turk J Pediatr Dis. 2014;1:32–4.
3. Hassan MN, Mohd Noor NH, Johan Noor SR, Sukri SA, Mustafa R, Luc Aster HV. Hemolytic disease of fetus and newborn due to maternal red blood cell alloantibodies in the Malay population. Asian J Transfus Sci. 2014;8(2):113–7.
4. Ree IMC, de Grauw AM, Bekker V, et al. Necrotizing enterocolitis in haemolytic disease of the newborn: a retrospective cohort study. Vox Sang. 2020;115(2):196–201.
5. Figueras-Aloy J, Rodríguez-Miguélez JM, Iriondo-Sanz M, Salvia-Roiges MD, Botet-Mussons F, Carbonell-Estrany X. Intravenous immunoglobulin and necrotizing enterocolitis in newborns with hemolytic disease. Pediatrics. 2010;125(1):139–44.
6. Gephart SM. Transfusion-associated necrotizing enterocolitis: evidence and uncertainty. Adv Neonatal Care. 2012;12(4):232–6.

Ana Gutiérrez-Vélez[a], Amaia Merino-Hernández[b,*], Isabel Pescador Chamorro[a], Manuel Sánchez Luna[a], Jorge Huerta-Aragonés[c]

[a] *Unidad de Neonatología, Servicio de Pediatría, Hospital General Universitario Gregorio Marañón, Madrid, Spain*
[b] *Servicio de Pediatría, Hospital General Universitario Gregorio Marañón, Madrid, Spain*
[c] *Unidad de Oncohematología, Servicio de Pediatría, Hospital General Universitario Gregorio Marañón, Facultad de Medicina, Universidad Complutense de Madrid, Instituto de Investigación Sanitaria Gregorio Marañón (IiSGM), Madrid, Spain*

[*] Corresponding author.
E-mail addresses: ana.gutierrez@salud.madrid.org (A. Gutiérrez-Vélez), amaia.merino1@gmail.com (A. Merino-Hernández), isapesca@hotmail.com (I.P. Chamorro), msluna@salud.madrid.org (M.S. Luna), jorge.huerta@salud.madrid.org (J. Huerta-Aragonés).

https://doi.org/10.1016/j.anpede.2022.10.001

Ecthyma gangrenosum as an initial manifestation of acute lymphoblastic leukemia

Ectima gangrenoso como manifestación inicial de leucemia linfoblástica aguda

Dear Editor,

Ecthyma gangrenosum (EG) is a cutaneous lesion frequently associated with infection by *Pseudomonas aeruginosa*.[1] It usually affects immunocompromised patients, although its presence is rate at the time of diagnosis of acute lymphoblastic leukaemia (ALL).[2] We present 2 cases of EG as the initial manifestation of ALL.

Case 1. Boy aged 19 months, with no history of interest, brought to the emergency department with high fever of 3 days' duration and a skin lesion measuring 1 × 2 cm with an ulcerated centre surrounded by a necrotic scab in the external surface of the right leg. The salient blood test results were pancytopenia (haemoglobin, 5.2 g/dL; platelet count, 60 000/mm^3; neutrophil count, 450 cells/mm^3) and a lymphoblast percentage of 78%, suggestive of ALL, with elevation of acute phase reactants (C-reactive protein [CPR], 300 mg/L; procalcitonin [PCT], 33 ng/mL). Broad-spectrum antibiotherapy was initiated with intravenous piperacillin–tazobactam, amikacin and vancomycin following collection of a wound swab and blood sample for culture.

The bone marrow test confirmed the diagnosis of common B-cell ALL with hyperdiploidy. The lumbar puncture was traumatic with cerebrospinal fluid without blasts (CNS 2t). Additional tests (chest radiograph, echocardiography, abdominal ultrasound, cranial magnetic resonance imaging and funduscopic examination) only detected splenomegaly. Remission induction therapy was initiated according to the LAL/SEHOP-PETHEMA-2013 protocol for intermediate risk patients. The patient was reclassified as high risk on day 8 due to poor response to prednisone (>1000 blasts/mm^3 in peripheral blood). Multisensitive *P. aeruginosa* was isolated from the would culture, but the blood culture was negative. Treatment with vancomycin and amikacin was discontinued and the patient completed the 10-day course with piperacillin/tazobactam.

Local treatment started with surgical wound care with application of silver sulfadiazine every 48 h. However, the patient did not respond favourably and required negative pressure wound therapy followed by flap surgery at 40 days post diagnosis. To promote healing of the ecthyma, the patient received treatment with granulocyte colony-stimulating factor (G-CSF) and a healthy-donor granulocyte transfusion.

The outcome was favourable, with a short delay in initiation of chemotherapy. The patient achieved complete remission on day 33, with minimal residual disease (0.01%).

Case 2. Girl aged 3 years, born preterm at 34 weeks' gestation, brought to the emergency department with high fever of 4 days' duration and vomiting, decreased feeding, refusal to walk, pallor, asthenia and dizziness. On examination, she appeared septic, with hepatosplenomegaly and an exudative cutaneous lesion measuring 1 × 1 cm in the scalp. Blood tests revealed pancytopenia (haemoglobin, 3.8 g/dL; platelet count, 79 000/mm^3; neutrophil count, 0 cells/mm^3) and an atypical lymphoblast percentage of 2%, suggestive of an acute lymphoproliferative process, with elevation of acute phase reactants (CPR, 282.7 mg/L; PCT, 18.19 ng/mL) and coagulopathy. Sepsis was suspected, leading to initiation of empiric antibiotherapy with intravenous piperacillin-tazobactam, vancomycin and amikacin following collection of a wound swab and blood sample for culture. The bone marrow test confirmed the diagnosis of acute leukaemia, more specifically, common B-cell ALL with hyperdiploidy. The patient underwent a cranial computed tomography scan and funduscopic examination on an emergency basis, the results of which were normal. The cerebrospinal fluid analysed at 3 days from onset due to coagulopathy and instability associated with sepsis was traumatic but without blasts (CNS 2t). The abdominal ultrasound revealed hepatosplenomegaly; and the results of all other tests were normal.

Remission induction therapy was initiated according to the LAL/SEHOP-PETHEMA-2013 protocol for standard risk patients. Multisensitive *P. aeruginosa* was isolated from the wound sample, while the blood culture was negative. The patient required wound care every 48 h, administration of G-CSF, enzymatic debridement and negative pressure wound therapy (single-use PICO system), which achieved a favourable response. The assessment of ALL on days 8 and 15 showed improvement. The patient achieved morphological remission on day 33 with minimal residual disease (<0.01%) (Figs. 1 and 2).

The presence of EG in seemingly immunocompetent patients requires an exhaustive investigation to rule out