Passive Transfer of Hepatitis B Antibodies through Intravenous Immunoglobulin in a Neonate

INTRODUCTION
As intravenous immunoglobulin (IVIG) increases its clinical application it becomes increasingly important for attending physicians to be alert to the risk of passive transfer of antibodies, especially in patients whose seropositivity may lead to unnecessary therapies or even prevent essential treatments. Even though this phenomenon has already been described in literature,1–4 it remains little known. We report a case of a neonate with dilated cardiomyopathy who presented positive hepatitis B core antibodies after administration of IVIG.

CASE REPORT
Male infant, six months old at the time of this report, with no relevant family history. Pregnancy was uneventful, except for an obstetric ultrasound with left ventricular hyprevascularity focus at the 31th week, which disappeared at the 36th week. No fetal echocardiogram was performed. Maternal serologic screening for human immunodeficiency virus (HIV), hepatitis C virus (HCV), hepatitis B virus (HBV) and toxoplasmosis was negative, and she was immune to virus (HIV), hepatitis C virus (HCV), hepatitis B virus (HBV) and toxoplasmosis was negative, and she was immune to rubella and cytomegalovirus. Delivery occurred at term and diagnosed with dilated cardiomyopathy, presented positive hepatitis B core antibodies at 12 days of life. Exclusion of hepatitis B infection was mandatory as it would be a contraindication to heart transplant. Passive transfer of antibodies was confirmed at 44 days of age, after seroreversion of hepatitis B core antibodies. Passive transfer of antibodies after intravenous immunoglobulin infusion can lead to a misleading diagnosis if not recognized. In our patient it could have been especially harmful had it prevented heart transplant. Screening for hepatitis B should be performed at least 1 month after intravenous immunoglobulin infusion.

Keywords: Cardiomyopathy, Dilated; Hepatitis B Antibodies; Immunoglobulins, Intravenous/adverse effects; Infant, Newborn

RESUMO
A transferência passiva de anticorpos secundária à infusão de imunoglobulina endovenosa é um efeito secundário raro, mas importante, que pode levar a um diagnóstico e decisões terapêuticas erradas. Nunca foi descrito num recém-nascido. Um recém-nascido do sexo masculino, vacinado contra a hepatite B e diagnosticado com miocardiopatia dilatada, apresentou anticorpos anti-core do vírus da hepatite B aos 12 dias de vida. A exclusão da infecção por hepatite B foi obrigatória, pois seria uma contra-indicação ao transplante cardíaco. A transferência de anticorpos através de imunoglobulina endovenosa foi confirmada aos 44 dias de idade, após sero-reversão dos níveis de anticorpos anti-core do vírus da hepatite B. A transferência passiva de anticorpos após a infusão de imunoglobulina endovenosa pode levar a um diagnóstico errado se não for reconhecida. Neste doente poderia ter sido especialmente prejudicial caso tivesse impedido o transplante de coração. O rastreio para hepatite B deve ser realizado pelo menos um mês após a infusão.

Palavras-chave: Anticorpos Anti-Hepatite B; Cardiomiopatia Dilatada; Imunoglobulinas Intravenosas/efeitos adversos; Recém-Nascido

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normal at the 10th and 34th days of life. He had no nutrition- al deficiencies. An extensive panel of viral serologies was requested for exclusion of a viral cause (coxsackie, adenovirus, echovirus, influenza A and B virus, parvovirus B-19, herpes virus 6, Epstein-Barr virus, cytomegalovirus, HIV 1 and 2, HCV), which was all-negative. Serology for HBV was repeated at the 12th day of life, one day after admin- istration of IVIG, due to insufficient volume of the previous blood sample taken at the eighth day of life. He had positive anti-HBs and anti-HBc antibodies. Complete serology was performed the day after for confirmation: there were again positive anti-HBs and anti-HBc antibodies, negative HBs antigen, absence of IgM class anti-HBc antibodies, HBe antigen and anti-HBe antibodies. At 44 days of age, anti- HBc antibodies were negative (Table 1) and anti-HBs anti- bodies were positive, as expected in an infant with immunity to HBV infection after vaccination. The echocardiogram at two months of life showed severe left ventricular dilation with depressed systolic function and he was placed on the heart transplant waiting list. He was successfully transplant- ed at three months of age.

**DISCUSSION**

We present a case of a newborn in whom administration of IVIG interfered in the serology result for hepatitis B. This is a rare event and has never been described at such an early age and in this particular setting. Its recognition was key as he was a patient who could need cardiac transplanta- tion and immunosuppressive therapy, with the consequent risk of viral reactivation. This reactivation can occur even in persons who are anti-HBs positive, although with a lower risk. As an example, in a prospective study evaluating the risk of HBV reactivation in 150 antigen HBs negative and anti-HBc positive patients undergoing chemotherapy with a rituximab-containing regimen for lymphoma, HBV reac- tivation occurred in nine of the 116 patients (8%) who were positive for anti-HBs at baseline and eight of the 35 (23%) who were negative for anti-HBs.5

Dilated cardiomyopathy (DCM) is defined by dilation and systolic dysfunction of the left ventricle (LV) or both ventricles not explained by abnormal ventricular filling conditions (e.g., arterial hypertension, valvular disease) or coronary disease.6 Its etiology includes idiopathic DCM, familial DCM, viral, autoimmune or toxic myocarditis and metabolic disease. The most common cause of acquired DCM is viral myocarditis. Therapy in the neonatal period is extrapolated from children and adult data.7 One of the possible treatments of viral myocarditis DCM is intravenous immunoglobulin infusion.8 Treatment of DCM with refractory heart failure is cardiac transplantation.9

Arnold et al described an abnormally high rate of anti- HBc seropositive patients during a rituximab clinical trial.1 The authors concluded that 10 out of the 11 seropositive patients had received IVIG therapy in the previous four weeks and found that seven of these patients reverted to seronegative after repeated testing. The patients were screened for HBV infection due to the risk of hepatitis B reactivation after immunosuppressive therapy. The authors stated that, in order to avoid misleading results, anti-HBc antibodies should only be evaluated either before or three months after the administration of IVIG. In our case, hep- atitis B core antibodies were negative one month after IVIG infusion. We conducted a brief review of the literature which showed two more clinical cases23 and a prospective study4 that also reported this phenomenon.

Our patient, a newborn with no identifiable cause for infection since his mother was hepatitis B seronegative and had no significant changes in liver markers, had a likely exogenous source of hepatitis B core antibodies, confirmed by their seroreversion at 44 days of age. Hepatitis B surface antibodies were and remained positive, as expected after successful vaccination.

Information provided by the manufacturer of the drug used, Octagam® 5%,10 states that it is composed of ≥ 96% human IgG and prepared by fractionating fresh frozen plasma donated by the general population. Each preparation is made from a plasma pool of not less than 3500 dona- tions. General measures to avoid transmission of infectious agents through the product include selection of donors, screening of individual donations and pooling of plasma for specific markers of infection, and inclusion of steps for inac- tivation and viral clearance. Viral inactivation of the product is carried out using the solvent/detergent method with a mix- ture of octoxynol (triton X-100) and TnBP (tri n-butyl phos- phate) and a specific treatment with pH 4. The final product is tested for HBs antigen and HIV 1/2 antibodies. It is known that the infectious risk with immunoglobulin administration is extremely low.11 The requirements for donor screening and infectious disease testing are generally stringent and the manufacturing process normally includes 1 to 2 steps of viral inactivation.10 The manufacturer’s information further states that, with the administration of IVIG, various anti- bodies may be passively transferred to the patient’s blood, which may lead to positive serological tests. The half-life of the drug is 36 to 40 days, which agrees with the evolution of the patient’s serology (Table 1).

### Table 1 – Results from hepatitis B virus research

<table>
<thead>
<tr>
<th>Sample</th>
<th>23/01/2017 (8 days of life)</th>
<th>26/01/2017 (12 days of life – 1 day post IVIG)</th>
<th>09/03/2017 (44 days of life – 33 day post IVIG)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antigen HBs</td>
<td>Insufficient</td>
<td>Negative (0.45)</td>
<td>Negative (0.62)</td>
</tr>
<tr>
<td>Antibody anti-HBc</td>
<td>Negative (2.07)</td>
<td>Positive (0.03)</td>
<td>Negative (1.48)</td>
</tr>
<tr>
<td>Antibody anti-HBs</td>
<td>Positive (&gt; 1000)</td>
<td>Positive (202)</td>
<td></td>
</tr>
<tr>
<td>Antibody anti-HBc IgM class</td>
<td>Negative (0.08)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antigen HBe</td>
<td>Negative (0.10)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antibody anti-HBe</td>
<td>Negative (1.20)</td>
<td></td>
<td></td>
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</tbody>
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Retalho Livre Anterolateral da Coxa para Tratamento de Quelóide Esternal

Use of Anterolateral Thigh Free Flap in the Treatment of a Sternal Keloid

Tiago GUEDES¹, Gustavo COELHO¹, João GUIMARÃES¹, Horácio COSTA¹

RESUMO
As cicatrizes hipertróficas e quelóides representam distúrbios cicatriciais hiperproliferativos que podem ter um impacto significativo na vida dos doentes. Os autores apresentam o caso de um doente de 53 anos, com uma cicatriz quelóide na região esternal após exérese de um quisto sebáceo e múltiplas sessões de infiltração de corticóide, com um agravamento marcado da lesão. O doente foi submetido a exérese do quelóide e reconstrução do defeito com retalho livre fasciocutâneo anterolateral da coxa (anterolateral thigh flap — ALT). O pós-operatório imediato e tardio decorreu sem intercorrências, sem sinais de recidiva. O tratamento de quelóides esternais passa, nas dimensões e localização da cicatriz, a sua excisão provocou um defeito extenso, sendo necessária a transferência microcirúrgica.

Palavras-chave: Coxa; Esterno; Procedimentos Cirúrgicos Reconstrutivos; Quelóide; Retalhos de Tecido Biológico/transplantação de tecidos para cobertura completa, minimizando a tensão na região esternal.

ABSTRACT
Hypertrophic and keloid scars represent hyperproliferative disorders that can have a significant impact on patients’ lives. The authors present the case of a 53-years-old male with a sternal keloid after excision of a sebaceous cyst and multiple sessions of steroid infiltration, with worsening of the lesion. The patient underwent complete excision of the scar and reconstruction with an anterolateral thigh flap — ALT. The postoperative period was uneventful, with no signs of relapse. Keloid scar treatment in sternal area implies a reconstruction with no tension, in order to avoid relapse. Treatment of this type of scars is complex and a challenge to the plastic surgeon.

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PROTECTION OF HUMANS AND ANIMALS
The authors declare that the procedures were followed according to the regulations established by the Clinical Research and Ethics Committee and to the Helsinki Declaration of the World Medical Association.

DATA CONFIDENTIALITY
The authors declare having followed the protocols in use at their working center regarding patients’ data publication.

REFERENCES