clarifications, which have led to corrections with respect to
the information previously issued. In some cases, if the first
manufacturer’s information had been considered correct,
the consequence of the administration of the drug in an
HFI patient could have had serious consequences on his
health. We believe there is a necessity of a review process
on the contents of the label in a coordinated way between
regulatory agencies and the companies that manufacture
and/or market these medicines.

References
1. Izquierdo-García E, Moreno-Villares JM, León-Sanz M. Edulco-
rantes en pacientes con intolerancia hereditaria a la fructosa.
2. Ruiz Pons M. Errores congénitos del metabolismo de la fructosa.
In: Sanjurjo P, Baldellou A, editors. Diagnóstico y tratamiento
de las enfermedades metabólicas hereditarias. 3ª ed. Madrid:
3. Directiva 2001/111/CE del Consejo, de 20 de diciembre del 2001,
relativa a determinados azúcares destinados a la alimentación
humana. Diario Oficial de las Comunidades Europeas, 12 de enero
del 2002.
4. Información sobre los excipientes en el etiquetado, prospecto
y ficha técnica de los medicamentos de uso humano. Circular
número 2/2008 de la Agencia Española del Medicamento y Pro-
ductos sanitarios (AEMPS).
5. Real Farmacopea Española. 32 ed. Madrid: Ministerio de Sanidad,
Servicios Sociales e Igualdad; 2005.
6. Real Decreto 299/2009 de 6 de marzo. Boletín Oficial del Estado,
nº. 68, de 20 de marzo del 2009. Normas de identidad y pureza
de los edulcorantes utilizados en los productos alimenticios.

Elsa Izquierdo-García a,* , Ismael Escobar Rodríguez a ,
José Manuel Moreno-Villares b , Irene Iglesias Peinado c

a Servicio de Farmacia, Hospital Universitario Infanta
Leonor, Madrid, Spain
b Unidad de nutrición clínica, Hospital Universitario 12 de
Octubre, Madrid, Spain
Variación hospitalaria, Universidad Complutense de
Madrid, Spain

C Corresponing author.
E-mail address: elsa.izquierdo@salud.madrid.org
(E. Izquierdo-García).
2341-2879 © 2016 Asociación Española de Pediatría. Published by Elsevier
España, S.L.U. All rights reserved.

Role of nuclear medicine in the
differential diagnosis of bone
infarction and osteomyelitis in
drepanocytosis

Papel de la medicina nuclear en el diagnóstico
diferencial entre infarto óseo y osteomielitis
en el contexto de drepanocitosis

Dear Editor:

Sickle cell disease is an autosomal recessive disease in
which red blood cells with abnormal haemoglobin S take
on a sickle shape, causing obstruction of capillary blood
flow and haemolysis. 1 Vaso-occlusive crises with bone
involvement (bone infarction) are the most common clinical
manifestation, mainly in the humerus, tibia and femur. 2
Tissue devitalization after vaso-occlusive crises, the satu-
rating of macrophages with products derived from chronic
haemolysis and splenic dysfunction predispose to bone
infection, 1,2 and Salmonella is the most frequent causative
agent. 3 Clinical manifestations are similar in both cases
(tenderness, warmth, erythema and swelling) 1 and the
findings of conventional imaging techniques (radiography
and ultrasonography) are frequently inconclusive. In the
field of nuclear medicine, dual-tracer bone scintigraphy
(with diphosphonate and colloid tracers) is available for the
purpose of differential diagnosis.

We present the case of a boy aged 12 years with sickle
cell disease that visited the emergency department with
pain in the proximal region of the left tibia lasting 48 h in
the absence of trauma. The patient initially improved with
analgesic treatment (morphine hydrochloride) but wors-
ened on the third day, with exacerbation of pain, local
oedema and elevation of acute phase reactants and pro-
calcitonin. The patient did not have leukocytosis or fever
(although the absence of fever is infrequent, it has been
described to reach proportions of up to 22% of cases in some
series 1).

A radiograph and an ultrasound examination were
ordered due to the need to make a differential diagnosis
between bone infarction and osteomyelitis. Both showed
nonspecific inflammatory soft tissue changes in the anterior
region of the left tibia and neither allowed differentiation of
the disease. Empirical intravenous antibiotherapy was initi-
ated, and a bone scintigraphy was ordered.

The patient underwent a bone scintigraphy scan, with
capture of static images in the blood pool phase (at 5 min)
and the metabolic phase (2 h) following intravenous injec-
tion of 335 MBq of 99mTc-HDP. The images revealed increased
distribution in the vascular and interstitial compartment and
increased osteogenic activity in the left tibial tuberosity,
with very faint and diffuse tracer uptake in the two prox-
imal thirds of the ipsilateral tibial diaphysis, and no other
abnormalities in the rest of the examined structures. This

* Please cite this article as: Sandoval-Moreno C, Castillejos-
Rodríguez L, García-Alonso AM, Rubio-Gribble B, Penín-González FJ.
Papel de la medicina nuclear en el diagnóstico diferencial entre
infarto óseo y osteomielitis en el contexto de drepanocitosis. An
Bone and scintigraphy can be used to differentiate between osteomyelitis and bone infarction. Scintigraphy shows normal uptake in the tuberosity of the left tibia, with decreased uptake in the two proximal thirds of the ipsilateral tibial shaft. The scintigraphic pattern is compatible with osteomyelitis in the tuberosity of the left tibia and with bone infarction in the two proximal thirds of the ipsilateral tibial diaphysis.

Early in the course of disease, it is difficult to differentiate between osteomyelitis and bone infarction based on clinical or radiological features. Nevertheless, plain radiography is used as the initial imaging technique to rule out other diseases (tumours and fractures). The characteristic radiologic findings cannot be detected until at least 10 days have elapsed since the onset of symptoms.

An ultrasound examination may be useful in sites that can be accessed with this technique, mainly for the detection of collections and abscesses in soft tissue.

Dual-tracer bone scintigraphy can differentiate between bone infarction and osteomyelitis. On scintigraphy, osteomyelitis presents with increased tracer uptake (there may be decreased uptake in the early stages). Increased uptake is also observed in cases of bone infarction during the revascularization phase, starting from the third day from onset (uptake may be normal or decreased before the third day).

It is during the revascularization phase that bone marrow scintigraphy can differentiate between the two diseases, as bone infarction continues to exhibit decreased uptake, whereas osteomyelitis exhibits normal tracer uptake.

Bone marrow scanning targets the reticuloendothelial system of bone marrow, while bone scanning reflects the reparative osteoblastic response. Bone scintigraphy is abnormal in both osteomyelitis and bone infarction, whereas bone marrow scintigraphy is normal in osteomyelitis.

In the context of sickle-cell disease, it is important to take into account the medical history, as previous bone infarctions may continue to exhibit decreased uptake and it is not possible to determine whether they are new or old lesions by means of scintigraphy, which requires consideration of current manifestations and the previous history in their assessment.

In conclusion, currently available nuclear medicine techniques can be very useful, as dual-tracer bone scintigraphy makes possible the early differential diagnosis of bone infarction versus osteomyelitis through non-invasive means, which is important in children with sickle cell disease in whom both diseases overlap.

References

Cristina Sandoval-Moreno a,*, Lourdes Castillejos-Rodríguez a, M. Pilar García-Alonso a, Bárbara Rubio-Gribble b, Francisco Javier Penín-González a

* Corresponding author.
E-mail addresses: cristycsm@gmail.com, cristina.sandoval@salud.madrid.org (C. Sandoval-Moreno).

© 2016 Asociación Española de Pediatría. Published by Elsevier España, S.L.U. All rights reserved.