Letters to the Editor

Lymphadenopathy Syndrome in Systemic Lupus Erythematosus: Is It Kikuchi-Fujimoto Disease?  

*Síndrome poliadenopático en lupus eritematoso sistémico: ¿es la enfermedad de Kikuchi-Fujimoto?*  

To the Editor,

Lymphadenopathy syndrome is a common manifestation of systemic lupus erythematosus (SLE). In general, enlarged lymph nodes are small and can be found in the cervical, inguinal and axillary regions. Lymph node involvement is present in up to 25% of the patients and normally appears in the first stages of the disease or during relapses. The differential diagnosis of lymphadenopathy syndrome in SLE includes histiocytic necrotizing lymphadenitis or Kikuchi-Fujimoto disease (KFD), Castleman’s disease, syphilis, tuberculosis, sarcoidosis, infectious mononucleosis (Epstein–Barr virus [EBV]), cytomegalovirus, herpes simplex, human immunodeficiency virus (HIV), hepatitis B virus (HBV), hepatitis C virus (HCV), other infections and lymphoma. Kikuchi-Fujimoto disease, or histiocytic necrotizing lymphadenitis, is a rare clinical disorder characterized by lymph node involvement (generally cervical), fever, night sweats and leukopenia. It mainly affects young Asian women. It was first described by Kikuchi and Fujimoto in 1972. The associated mortality is increased by heart, lung and liver involvement. The exact cause of KFD is not yet known, but recent publications are inclined toward a viral infection (EBV and others) or an autoimmune disorder (an exaggerated immune response mediated by T cells). To diagnosis the disease, it is necessary to perform an excisional biopsy of the affected lymph nodes. The association between KFD and SLE is rare, and whether it is incidental or a clinical manifestation of SLE continues to be a matter of debate.

The coexistence of these 2 diseases is reported in 2 young SLE patients (cases nos. 1 and 2) and we describe another case of lymphadenopathy syndrome in SLE (case no. 3) in which the affected lymph node was studied by cytology rather than excisional biopsy (Table 1). In all 3 cases, the results of serological testing for HIV, HBV, HCV, EBV, cytomegalovirus, herpes simplex virus, rubella, toxoplasma, parvovirus B19, *Yersinia enterocolitica*, *Salmonella* and *Brucella* were negative, as were the results of interferon–γ release assays (IGRA) for all 3 patients.

Kikuchi-Fujimoto disease has been associated with SLE and other connective tissue diseases, such as antiphospholipid syndrome, Sjögren’s syndrome, relapsing polychondritis and autoimmune hepatitis. It is generally a benign disease that resolves spontaneously in 1–4 months, but cases with a poor outcome and

<table>
<thead>
<tr>
<th>Case no. 1</th>
<th>Case no. 2</th>
<th>Case no. 3</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Demographic</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>36</td>
<td>30</td>
</tr>
<tr>
<td>Sex</td>
<td>Female</td>
<td>Female</td>
</tr>
<tr>
<td>Race</td>
<td>Caucasian</td>
<td>Latin American</td>
</tr>
<tr>
<td><strong>Clinical manifestations</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cervical lymph node involvement</td>
<td>Arthritis</td>
<td>Night sweats</td>
</tr>
<tr>
<td>Asthenia</td>
<td>Asthenia</td>
<td>Fever</td>
</tr>
<tr>
<td><strong>Laboratory</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ANA</td>
<td>1/320</td>
<td>ANA</td>
</tr>
<tr>
<td>Anti-dsDNA:</td>
<td>417 IU/mL</td>
<td>Anti-dsDNA:</td>
</tr>
<tr>
<td>C3: 75 mg/dL</td>
<td>C3: 112 mg/dL</td>
<td>C3:</td>
</tr>
<tr>
<td>C4: 12 mg/dL</td>
<td>C4: 24 mg/dL</td>
<td>C4:</td>
</tr>
<tr>
<td><strong>Image</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cervical CT</td>
<td>Thoracoabdominal CT</td>
<td>Cervical CT</td>
</tr>
<tr>
<td><strong>Pathology</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cervical lymph node: lymphocytes with areas of necrosis at different stages of maturation</td>
<td>Supraclavicular lymph node: lymphocytes with areas of necrosis at different stages of maturation</td>
<td>Excision biopsy not performed</td>
</tr>
<tr>
<td>Numerous CD8-positive lymphocytes with TIA1+ cytotoxic granules (Fig. 1A–C)</td>
<td>Numerous CD8-positive lymphocytes with TIA1+ cytotoxic granules (Fig. 1D)</td>
<td>Malignancy ruled out using ultrasound-guided FNAC</td>
</tr>
<tr>
<td><strong>Treatment and outcome</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glucocorticoids</td>
<td>Glucocorticoids</td>
<td>Glucocorticoids</td>
</tr>
<tr>
<td>Lymph node involvement almost completely disappeared</td>
<td>Azathioprine</td>
<td>Lymph node involvement almost completely disappeared</td>
</tr>
</tbody>
</table>

ANA, antinuclear antibodies; CT, computed tomography; dsDNA, double-stranded DNA; FNAC, fine-needle aspiration cytology.

Biopsy
Luis
Findings
Miriam
José
expressing
56
to
the
excisional
experience
that
glucocorticoids
reveal
alternative
ment,
common
the
efficacious,
arquitectures,
paracortical
1.
identify
erythematos.
1.
presentation
CD8
the
disease
means
node.
diagnosis
splenomegaly,
that,
no
presence
of
the
discorder,
rate
that,
consist
areas,
described
or
nodes
hypothesis
and
maturation.
areas
reaches
function
in
the
fig.
But,
relationship
the
enlargement,
node.
TIA1
the
lymphocytes
node.
Hematol-eosin:
lymphocytes
with
areas
of
necrosis
at
different
stages
of
maturación.

Biopsy
of
the
affected
lymph
nodes
reveals
irregular
necrotized
regions,
mostly
in
the
paracortical
areas,
with
partial
or
complete
loss
of
the
follicular
architecture,
karyorrhexis
and
the
absence
of
neutrophils,
with
the
presence
of
transformed
lymphocytes
(immunoblasts)
around
the
necrotic
areas.
The
lesional
cells
have
also
been
reported
to
infiltrate
the
periportal
fibroadipose
tissue.9
Findings
that
are
not
common
in
KFD
are
skin
lesions,
mesenteric
lymph
node
involvement,
splenomegaly,
myalgia
and
parotid
swelling.

There
is
no
effective
treatment
but,
in
cases
without
complications
or
in
self-limiting
disease,
glucocorticoids
are
usually
efficacious,
as
in
the
3
cases
documented
here,
although
studies
reveal
that
the
rate
of
recurrence
of
the
disease
is
3%–4%.10

In
the
third
case,
excisional
biopsy
was
not
performed,
a
fact
that
means
that,
in
this
patient,
we
cannot
speak
of
histiocytic
corticizing
lymphadenitis.
However,
the
course
and
outcome
of
the
disease
are
consistent
with
that
possibility
(the
good
response
to
glucocorticoids
rules
out
an
infectious
or
malignant
disease).
The
early
diagnosis
is
fundamental
for
the
correct
management
of
the
disease,
and
the
association
with
SLE
requires
more
research.
Our
experience
supports
the
hypothesis
that
it
is
necessary
to
perform
excisional
biopsy
of
the
lymph
nodes
in
cases
of
lymphadenopathy
spleomegaly
in
SLE
that
have
not
been
diagnosed.
Thus,
not
only
is
it
necessary
to
exclude
malignancy
by
means
of
cytology;
the
best
alternative
is
to
completely
remove
the
lymph
node
in
attempt
to
identify
the
disorder,
because
the
therapeutic
approach
will
be
different
in
each
stage
depending
on
the
result(Fig.
1).

Conflicts
of
Interest

The
authors
declare
they
have
no
conflicts
of
interest.

References

1.
Shapira
Y,
Weinberger
A,
Wysenbeek
AJ.
Lymphadenopathy
in
systemic
lupus
erythematosus.
Prevalence
and
relation
to
disease
manifestations.
Clin
Rheumato-

tol.

2.
Gómez
Caballero
ME,
Martínez-Morillo
M.
A
woman
with
systemic
lupus
erythematosis
and
polyadenopathy.
Reumatol
Clin.

3.
Kikuchi
M.
Lymphadenitis
showing
focal
reticulum
cell
hyperplasia
with
nuclear
debris
and
phagocytois.
Nippon
Ketsueki
Gakkai
Zasshi.
1972;35:

4.
Fujimoto
Y,
Kojima
Y,
Yamaguchi
K.
Cervical
subacute
corticizing
lymphadeni-
tis.
A
new
clinicopathological
entity.
Naika.

5.
Rezayat
T,
Carroll
MB,
Ramsey
BC,
Smith
A.
A
case
of
relapsing
Kikuchi-Fujimoto
disease.
Case
Rep
Otolaryngol.
2013;2013:364795.

6.
Smith
LW,
Petri
M.
Diffuse
lymphadenopathy
as
the
presenting
manifestation
of
systemic
lupus
erythematosis.
J
Clin
Rheumatol.

7.
Soy
M,
Peynirci
H,
Bilgi
S,
Adali
MK,
Gürcü
S.
Kikuchi-Fujimoto
disease
coex-
istas
with
Sjögren
syndrome.
Clin
Rheumatol.

8.
Kamptak
T.
Fatal
Kikuchi-Fujimoto
disease
associated
with
SLE
and
hemophagocytic
syndrome:
a
case
report.
Clin
Rheumatol.
2008;27:
1073–5.

9.
Pilichowska
M,
Pinkus
JL,
Pinkus
GS.
Histiocytic
corticizing
lymphadenitis
(Kikuchi-Fujimoto
disease)
lesional
cells
exhibit
an
immature
dendritic
cell
phe-
notype.
Ann
J
Clin
Pathol.

10.
Dorfman
RF.
Histiocytic
corticizing
lymphadenitis
of
Kikuchi
and
Fujimoto.
Arch
Pathol
Lab
Med.

Tarek
Carlos
Salman-Monte,a,*
José
Pérez
Ruiz,a
Miriam
Almirall,b
Miguel
Ángel
Campillo
Ibáñez,a
Luis
Carlos
Barranco
Sanz,a
Jordi
Carbonell
Abelló,a

a
Rheumatology
Department,
Parc
de
Salut
Mar/Hospital
del
Mar,
IMIM,
Department
of
Medicine,
Universitat
Autònoma
de
Barcelona
(UAB),
Barcelona,
Spain

b
Pathology
Department,
Parc
de
Salut
Mar/Hospital
del
Mar,
Barcelona,
Spain

E-mail
addresses:
tareto4@gmail.com,
98383@parcdesalutmar.cat
(T.C.
Salman-Monte).

http://dx.doi.org/10.1016/j.reumae.2016.04.004
2173-5743/
©
2015
Elsevier
España,
S.L.U.
and
Sociedad
Española
de
Reumatología
y
Colegio
Mexicano
de
Reumatología.
All
rights
reserved.