CASE REPORT

Systemic lupus erythematosus and Hodgkin disease [version 1; referees: 1 approved, 1 approved with reservations]

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v1 **First published:** 18 Oct 2012, **1**:31 (doi: 10.12688/f1000research.1-31.v1)
Latest published: 18 Oct 2012, **1**:31 (doi: 10.12688/f1000research.1-31.v1)

Abstract

We report on the rare association of Hodgkin's disease with systemic lupus erythematosus. Four years after the diagnosis of systemic lupus erythematosus, the patient developed cervical mass and weight loss. Histological and subsequent clonality studies confirmed classical Hodgkin's lymphoma. The awareness of the association of Hodgkin's disease with systemic lupus erythematosus and its modes of presentation will help in the early diagnosis and management of such patients.

Open Peer Review

Referee Status: ✔ ?

	Invited Referees 1	2
version 1 published 18 Oct 2012	✔	? report

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2 **Frederic Geissmann**, Kings College London UK

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How to cite this article: Dhaou BB, Boussema F, Aydi Z *et al.* **Systemic lupus erythematosus and Hodgkin disease [version 1; referees: 1 approved, 1 approved with reservations]** *F1000Research* 2012, **1**:31 (doi: 10.12688/f1000research.1-31.v1)

Grant information: The author(s) declared that no grants were involved in supporting this work.

Competing interests: No competing interests were disclosed.

First published: 18 Oct 2012, **1**:31 (doi: 10.12688/f1000research.1-31.v1)

Editorial note:

Please note that the refereeing status of this article was changed from "indexed" to "[v1; ref status: approved 1, approved with reservations 1]".

When this article was first published, *F1000Research* was still in its beta phase; during this period articles that received any two of "Approved" or "Approved with Reservations" statuses from the reviewers were labelled as "indexed". When the journal was formally launched in January 2013, the requirements for indexing were tightened, and only articles that are given either two "Approved" or one "Approved" plus two "Approved with Reservations" statuses by the reviewers are labelled "indexed". The new criteria for "indexing" can still be met in the future if a new revised version receives the necessary approval status from the reviewers.

Introduction

Systemic lupus erythematosus (SLE) is associated with lymphoproliferative diseases such as Hodgkin's lymphoma (HL)[1]. Since there is considerable overlap between the features of SLE and HL there can be a great difficulty in diagnosing HL in the presence of SLE[1].

Case report

A 35-year-old woman was followed from 2002 for SLE with neuropsychiatric, renal and hematologic involvements. She was treated with only glucocorticoids with favourable outcomes. In April 2006, when she was under steroid treatment of 10 mg/day, she was admitted for cervical mass and weight loss. Physical examination showed a left indolent, fixed and elastic cervical adenopathy. The biological assessment was normal. Computerized tomography of the chest and abdomen showed a left basicervical mass expanded to the anterior and superior mediastinum. Magnetic resonance imaging was suggestive of a thymoma (Figure 1, Figure 2). The cervicotomy showed a supraclavicular mass. Histological and subsequent clonality studies confirmed classical Hodgkin's lymphoma (HL) of the nodular sclerosing type. Viral serology (for Epstein-Barr, herpes simplex, and herpes zoster) was negative. The diagnosis of Hodgkin's disease stage Ia was retained and the patient was transferred to hematological department where she was treated by chemotherapy (adriamycin, bleomycin, vinblastine and dacarbazine) with favourable outcomes. She is being currently followed in our department and is in remission of her lupus and Hodgkin's disease.

Discussion

The relative risk of hematologic malignancy is estimated to be 60% higher in patients with SLE than in the general population, the reason being unknown[1]. Of all hematologic cases reported in patients with SLE, the most common is non-Hodgkin's lymphoma followed by Hodgkin's disease, leukemia, and then multiple myeloma[1].

The initial presenting features of SLE and Hodgkin's disease are similar, with fever, weight loss, and peripheral lymphadenopathy seen in most cases[1]. Our patient presented with weight loss and cervical adenopathy.

Persistent large lymph nodes not responding to conventional therapy in SLE should be biopsied for alternative diagnosis (i.e., lymphoma)[1].

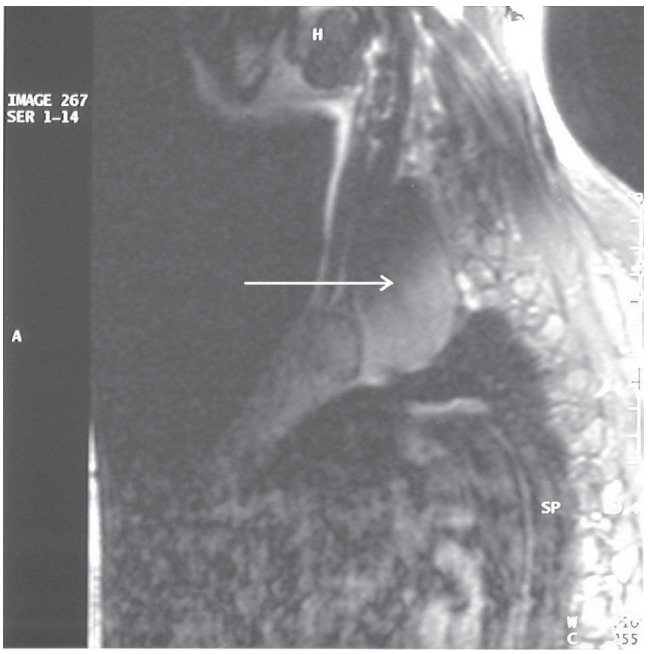

Figure 1. MRI thoracic sagittal suggestive of a thymoma.

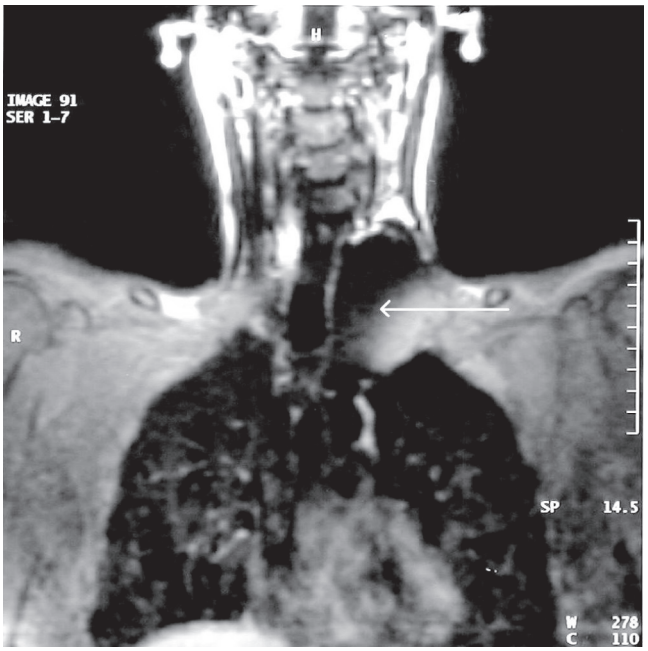

Figure 2. MRI thoracic coronal suggestive of a thymoma.

Several conditions and links have been identified that could potentially predispose patients with SLE to cancer (Table 1)[2,3].

A side-effect of immunosuppression is a possibility, as is intercurrent viral infection due to, for example, Epstein-Barr, herpes simplex, herpes zoster and polyoma viruses, which are potentially oncogenic. In our case, viral serology was negative.

Table 1. Potential links between systemic lupus erythematosus and malignancy.
* Growth and hormonal factors may play a role in autoimmunity as well as in malignancy[3].

- **Similarities between SLE immunologic disturbances and B-cell malignancies**
  - Abnormalities in survival, proliferation, and differentiation of lymphocytes
  - Similar defects in apoptosis
  - Chronic antigenic stimulation (can lead to lupus-like autoimmunity and B-cell lymphomas in mice models of graft-versus-host disease)
- **Growth and hormonal factors***
  - Insulin-like growth factor
  - Prolactin
  - Growth hormone
- **Viral triggers**
  - Epstein-Barr virus
- **Other**
  - Secondary Sjögren syndrome
  - Exposure to cytotoxic and immunomodulatory drugs used to manage SLE
  - Increased prevalence of traditional risk factors for malignancies (e.g., nulliparity, obesity) in patients with SLE

Patients who have had a renal transplant are known to have an increased risk of cancer[4]. They are, however, treated with much higher doses of immunosuppressive agents than patients with lupus. In the studies of Petterson *et al.*[5], Abu-Shakra[6] and Sultan *et al.*[7], the use of cytotoxic agents was not related to the occurrence of malignancy. Our patient was treated only with corticosteroids. It may be that the disease itself confers an increased risk. Patients with SLE have defects in both their cellular and humoral immune systems.

The mechanisms of hematologic malignancies[8] are thought to be related to the following:

- Failure or dysregulation of apoptosis as a result of mutated genes in SLE (Fas ligand).
- Accumulation of and mutations in B and T lymphocytes in the lymph nodes.
- T-cell immunodeficiency, allowing Epstein-Barr virus (EBV)-infected B-cell proliferation.
- Exposure to immunosuppressive medications (possible increased risk of EBV infection in patients with SLE)[9].

Large multicenter studies are required to adequately address the risk of developing malignancies in large cohorts of patients with SLE and to address issues such as associated risk factors and additional confounding factors, such as deprivation and exposure to therapy. The chance of detection of malignancy may vary due to factors such as access to health services, which vary widely and are not uniformly available, and may therefore underestimate the risk of malignancy.

Conclusion

SLE has been associated with increased frequency of neoplasia, lymphoma, leukaemia and epithelial tumours. Hodgkin's disease has been occasionally associated with SLE in adults. An awareness of the association of Hodgkin's disease with SLE and the modes of presentation will help in the early diagnosis and clinical management of such patients.

Author contributions

All authors participated in the completion of this work. They participated in the implementation of the clinical case and the proceeding discussion.

Competing interests

No competing interests were disclosed.

Grant information

The author(s) declared that no grants were involved in supporting this work.

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PubMed Abstract | Publisher Full Text

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Current Referee Status: ✔ ?

Version 1

Referee Report 12 November 2012

doi:10.5256/f1000research.206.r342

? **Frederic Geissmann**
Centre for Molecular and Cellular Biology of Inflammation, Kings College London, London, UK

The authors described a case of association of Hodgkin's disease with systemic lupus erythematosus. This clinical report is interesting, if not novel, and reminds the clinician that persistent lymphadenopathy in SLE patients, can be due in some case to a curable malignancy.

In my opinion, the report is too preliminary to allow the reader to conclude independently on the validity of the author's findings. A revised version of this report should include the following points;

1. To support their diagnosis and their conclusion, the authors should describe and document the clonality studies performed.
2. A selection of histological/immunohistochemical stainings on which the diagnosis was based would also be useful.
3. One proposed mechanism for the association of of Hodgkin's disease with systemic lupus erythematosus is immunosupression due to treatment of SLE. The authors mentioned and discussed that viral serology for Epstein-Barr virus was negative, but did they investigate whether the EBV genone could be detected in pathological samples or the blood of the patients?
4. Table 1 should be referenced and completed, so that reader can appreciate a) whether the 'Potential links between systemic lupus erythematosus and malignancy' rely on documented evidence, b) the level of that evidence, and c) the nature of the malignancies associated with SLE (i.e. Hodgkin's disease only, or other cancers).

I have read this submission. I believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Competing Interests: No competing interests were disclosed.

Referee Report 30 October 2012

doi:10.5256/f1000research.206.r341

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I have read this submission. I believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Competing Interests: No competing interests were disclosed.