Letters to the Editors

Detection of anti-neutrophil cytoplasmic and antinuclear autoantibodies favouring misdiagnoses in 5 cases of Erdheim-Chester disease

Sirs,

Erdheim Chester disease (ECD) is a rare non-Langerhans cell histiocytosis affecting one or multiple organs (1). Although any organ can be the first diagnosis in a patient of the central nervous system (CNS), orbit, heart, lung, retroperitoneum, bones and skin is most frequently encountered in ECD (1-4). Classification of ECD according to predominant affection of one organ system or multisystem ECD is used (3). A high prevalence of activating kinase mutations such as BRAF V600E suggests clonal expansion of histiocytes as the underlying cause of ECD (1, 5). A marked infiltration with foamy monocloned CD68-positive, CD1a and S100 negative histiocytes is the distinctive histopathologic feature of ECD (1). Diagnostic criteria include characteristic histological findings and evidence of skeletal abnormalities on x-ray and bone scintigraphy (6). Between March 2015 and 2017, we diagnosed five consecutive cases of loco-regionally dominant ECD (Table I). Isolated CNS lupus had been initially discussed as a possible differential diagnosis in patient 1 before. In patients 2, 4 and 5, the preexisting diagnoses were undifferentiated connective tissue disease or Sjögren’s syndrome. Finally, ANCA-associated vasculitis had formerly been assumed in patient 3. All patients had insufficiently responded to previous treatment with either prednisolone alone or in combination with methotrexate or azathioprine. Based upon reevaluation of the patients’ medical history, their disease course and request of specified immunohistochimistry and BRAF V600E mutation analysis of resected tissues, we reclassified the disease as ECD in patients 1–5. Time from first manifestation to diagnosis of ECD was 107 months (median; range 3–228 months) in our cohort as compared to a recently reported mean time to diagnosis of 51 months (2). The rarity of ECD often impedes a timely diagnosis and requires a high degree of suspicion. A delay before diagnosis of up to 25 years was noted in another study (6). Incidental detection of antinuclear autoantibodies (ANA) and different antigen-specificities of ANCA including myeloperoxidase (MPO) and proteinase 3 (PR3) was negative in our patients. In another case series, autoimmune diseases were suspected in 27% and vasculitis 22% of the patients; other misdiagnoses were sarcoidosis, lymphoma, and brain- and bone-cancer (2). After reclassification and diagnosis of ECD in our patients, we followed the consensus guidelines for the diagnosis and management of ECD (3). Remission was induced with interferon-α in four of our patients, while an increase of the azathioprine dosage was sufficient to control disease in the fifth. Interferon-α and anti-cytokine directed therapies have been recommended as first-line treatment in ECD (3, 7). Vemurafenib may represent an alternative in those >50% of patients with V600E BRAF mutation (8).

F. ÖZDEN1, MD
S. SCHINKE1, MD
C. THORNS2, MD
T. ECKEY1, MD
K. DALHOFF2, MD
T. F. MÜNTE1, MD
V. TRONNIEP1, MD
J. Y. HUMRICH1, MD
G. RIEKEMASTEN1, MD
P. LAMPRECHT1, MD

1Department of Rheumatology and Clinical Immunology, University of Lübeck; 2Institute for Pathology, Cath. Mary’s Hospital, Hamburg; 3Institute for Neuropathology, University of Lübeck; 4Department of Internal Medicine III – Pulmonology, University of Lübeck; 5Department of Neurology, University of Lübeck; 6Department of Neurosurgery, University of Lübeck, Germany.

Please address correspondence to: Dr Filiz Özden, University of Lübeck, Ratzeburger Allee 160, 23538 Lübeck, Germany. E-mail: filiz.oezden@uksh.de

Competing interests: none declared.

© Copyright CLINICAL AND EXPERIMENTAL RHEUMATOLOGY 2018.

References

Table I. Clinical manifestations in 5 patients with Erdheim Chester disease (ECD).

<table>
<thead>
<tr>
<th>Patient</th>
<th>Final diagnosis</th>
<th>Auto-antibody</th>
<th>BRAF V600E mutation</th>
<th>Surgical procedures before diagnosis</th>
<th>Treatment following diagnosis of ECD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient 1</td>
<td>CNS dominant ECD</td>
<td>ANA 1:10240</td>
<td>Negative</td>
<td>Resection of cerebral lesion</td>
<td>Interferon-α</td>
</tr>
<tr>
<td>Patient 2</td>
<td>Cardiac dominant ECD</td>
<td>ANA 1:320, centromere ab.</td>
<td>Positive</td>
<td>Pericardiocentesis andectomy</td>
<td>Interferon-α</td>
</tr>
<tr>
<td>Patient 3</td>
<td>Orbital-craniofacial dominant ECD</td>
<td>P-ANCA 1:160</td>
<td>Negative</td>
<td>Repetitive resections of nasolabial tumescence</td>
<td>Interferon-α</td>
</tr>
<tr>
<td>Patient 4</td>
<td>Orbital-craniofacial dominant ECD</td>
<td>ANA 1:320</td>
<td>Negative</td>
<td>Resection of orbital tumescence</td>
<td>Azathioprine</td>
</tr>
<tr>
<td>Patient 5</td>
<td>Orbital-craniofacial dominant ECD</td>
<td>ANA 1:160</td>
<td>Negative</td>
<td>Resection of orbital tumescence</td>
<td>Interferon-α</td>
</tr>
</tbody>
</table>

ANA: anti-nuclear autoantibody; P-ANCA: perinuclear anti-neutrophil cytoplasmic autoantibody.