Intravascular large cell lymphoma (ILCL) is a diagnostic challenge, with neurological, cutaneous and constitutional symptoms. The natural history is usually an evolution to a comatose state. As invasive procedures are usually required for diagnosis, recognizing the typical clinical pattern is critical since an effective treatment is available. **Method:** After an extensive literature review of the subject, we report a case of ILCL, analyzing clinical, laboratory, radiological and pathological data. We will also give a special attention to the clinical picture of a conus medullaris (CM) lesion with subsequent encephalopathy in the same patient. **Results:** We report here a 61-year-old woman with a paraplegia caused by a CM lesion, evolving about one year latter to encephalopathy and eventual coma, with the diagnosis of ILCL confirmed by autopsy. The present case is similar to eight other cases in literature who had CM lesion associated with ILCL, knowing that 80-90% of these patients will eventually evolve to encephalopathy without treatment. **Conclusions:** ILCL is a recognized but rare cause of coma. Diagnosing it is tremendously important since it is fatal if left untreated. We propose that this specific picture (conus medullaris lesion, eventually evolving to encephalopathy) is quite characteristic and will directly result in better outcome if recognized.
skilled physicians. Recognizing a typical clinical pattern evoking ILCL could help physicians to be more aware of this condition, thus resulting in earlier diagnosis. This is critical because an effective treatment is available.7,8

CASE REPORT

A 61-year-old woman presented in December 2002 with recent headache and scotomas mimicking migraine, superimposed on a four month history of progressive paraparesis and bowel and bladder incontinence. She also reported a 20 pound weight loss in the last few months. The initial physical exam showed bilateral leg paresis (with strength about 3/5), requiring the use of a walker. Anal tone was diminished and sensory exam of lower limbs showed symmetrical diminution of all sensation (touch, cold, pinprick, vibration). There were no cognitive or upper motor neuron deficits. Spinal magnetic resonance imaging (MRI) showed a gadolinium-enhancing lesion in the conus medullaris (CM) compatible with myelitis, with another lesion at T11-T12 (Figure 1). A complete work-up, including brain MRI, visual evoked potentials and lumbar puncture for cerebrospinal fluid analysis (CSF), was done and showed no relevant abnormalities except for high CSF protein at 0.56 g/L (0.15 – 0.40) and isolated elevated serum lactate dehydrogenase (LDH) at 381 U/L (90 – 200). The CSF oligoclonal banding was absent.

Following dexamethasone treatment she improved greatly and was able again to walk without help. She was discharged with a weaning regime of dexamethasone. Her blood LDH remained elevated afterward (1923 U/L, normal 313 – 618 in another laboratory) and the sedimentation rate (ESR) was 55 mm/h (normal < 10). She relapsed in July 2003 and consulted in another hospital where they initiated a mitoxantrone treatment (8 mg/m² IV at each four weeks for three times, thereafter 12 mg/m² every three months with a maximum of 140 mg/m²) although she did not fill the criteria for multiple sclerosis. No noteworthy improvement came from that treatment. She also presented deep venous thrombosis of the legs during this period and was treated with warfarin.

She came back to our center in May 2004 because of a newly appearing confusional state (paranoid remarks and lack of words) combined with hyperthermia, neutropenia (1.41 X 10⁹/L, normal >2) and significant weight loss (80 pounds in the last year). This febrile neutropenia did not respond to antibiotics. The new laboratory results showed no meaningful data with the exception of an evolving thrombocytopenia (from 113 X 10⁹/L to

Figure 1: (A) Sag T1 FS gadolinium-enhanced MRI showing an enhancing conus medullaris lesion (arrow) in December 2002. (B) The same lesion in Sag T2.

Figure 2: (A) Normal axial FLAIR brain MRI at the time of presentation with encephalopathy on May 16, 2004. (B) Axial FLAIR brain MRI showing multiple hyperintense lesions when the patient became comatose on May 23, 2004. (C) Ax T1 FS gadolinium-enhanced brain MRI without significant enhancement the same day.
### Table 1: Cases of ILCL reported in literature with conus medullaris involvement, both clinically and paraclinically (MRI and/or autopsy)

<table>
<thead>
<tr>
<th>Age</th>
<th>Presentation</th>
<th>Evolution</th>
<th>Treatment</th>
<th>ILCL diagnosis</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>78</td>
<td>Paraparesis</td>
<td>Death from cardiogenic shock 1 month later</td>
<td>None reported</td>
<td>Autopsy</td>
<td>16*</td>
</tr>
<tr>
<td></td>
<td>Pain/hypoesthesia of sacral dermatome</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>43</td>
<td>Legs pain</td>
<td>Confusion</td>
<td>1st: Steroids&lt;br&gt;2nd: Methotrexate, Dexamethasone</td>
<td>Brain biopsy</td>
<td>17</td>
</tr>
<tr>
<td></td>
<td>Double incont.&lt;br&gt;Headache</td>
<td>Death</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>63</td>
<td>Paraparesis</td>
<td>Death from gastrointestinal bleeding</td>
<td>1st: Immunoglobulins, steroids&lt;br&gt;2nd: Foscavir</td>
<td>Autopsy</td>
<td>18</td>
</tr>
<tr>
<td></td>
<td>Urinary incont.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>71</td>
<td>Confusion</td>
<td>Then death from respiratory distress</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>64</td>
<td>Backache</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Urinary retention</td>
<td></td>
<td></td>
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<tr>
<td>64</td>
<td>Paraparesis</td>
<td>Death from abdominal sepsis</td>
<td>1st: Steroids&lt;br&gt;2nd: Cyclophosphamide + ACVB&lt;br&gt;3rd: Methotrexate + Holoxan-VPr6</td>
<td>Muscle + telangiectasia biopsy</td>
<td>20</td>
</tr>
<tr>
<td>41</td>
<td>Urinary incont.</td>
<td>Paraplegia, Seizure, Confusion</td>
<td>1st: Steroid&lt;br&gt;2nd: Cyclophosphamide</td>
<td>Autopsy</td>
<td>21</td>
</tr>
<tr>
<td></td>
<td>Impotence&lt;br&gt;Genital sens. Loss</td>
<td>Death</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>71</td>
<td>TIA</td>
<td>Confusion</td>
<td>1st: Steroid&lt;br&gt;2nd: MBVP</td>
<td>Brain biopsy</td>
<td>22</td>
</tr>
<tr>
<td></td>
<td>Paraplegia&lt;br&gt;Urinary incont.</td>
<td>Seizure</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>63</td>
<td>Confusion</td>
<td>Double incont.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Paraparesis</td>
<td>Death</td>
<td>Immunoglobulins&lt;br&gt;Steroids&lt;br&gt;Azathioprine</td>
<td>Autopsy</td>
<td>23</td>
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</table>

Legend: ACVB = adriamycin, cyclophosphamide, vindesine, bleomycin, Incont. = Incontinence, MBVP = methotrexate etoposide BICNU solumedrol, Ref = Reference. * No spinal cord MRI was done for this cases. Others had positive CM lesion on MRI. ** Informations taken from the abstract (article in Japanese). Note: Another article reported a patient with CM syndrome, but here with no paraclinical confirmation (MRI or autopsy).
be considered among causes of CM lesion (Table 2). We propose that the eventual outcome will be better if therapy is started before the occurrence of cognitive dysfunction. Also, because encephalopathy is usually a late manifestation (37% at diagnosis and 82% before death), this kind of evolution (CM involvement evolving to an encephalopathy), as in our case, seems characteristic of ILCL.

After central nervous system dysfunction, the most common features are constitutional symptoms (fever, weight loss, asthenia), found in 50% of patients and which herald, as in our case, lymphoproliferative disorder. Cutaneous manifestations (nodules, indurate plaques, purpura, telangiectasia) are found in one out of three cases. There are conflicting reports about the possible association of neurological and cutaneous symptoms in the same patient. Chapin reported only two cases with skin manifestations among his 64 neurological ILCL cases, but other series revealed a 20% association. Nevertheless, searching for these kinds of abnormalities is important because a biopsy of these lesions can often give the diagnosis. Other organ dysfunction has been described (lungs, adrenals, prostate, spleen) but they are extremely rare, despite the very high incidence of involvement of these organs at autopsy. Notably lymphadenopathy was absent.

Paraclinical findings usually encountered in this condition are elevated blood LDH without alteration of the remaining liver function tests (85 – 90%), elevated ESR (80%) and CSF protein with presence of oligoclonal bands (only reported in a nine patients series with seven of them positive). In our case, blood LDH and CSF protein were increased on the first investigation. Anemia (45%) and thrombocytopenia (23%, as in our case) are often found. The relative lack of malignant cells in CSF cytology (3%) and blood smears (5%) probably occurs because the abnormal cells cling to the vascular endothelium rather than passing through the vessel wall. Bone marrow biopsy may be very useful according to some, but is seldom positive according to another series, with only one out of eight patients positive. Cerebral ischemic damage is usually well shown on neuroimaging studies and cerebral angiography can give exactly the same appearance as seen in vasculitis. Finally, an increase of adrenal gland volume is another finding that raises the possibility of ILCL.

Considering all these pitfalls, ILCL antemortem diagnosis is rarely made, as in our case. In this regards, even if cerebral or meningeal biopsy near a documented lesion (which is considered sufficient by some authors) has a sensitivity of 33 to 100%, each should be considered since with a tissue diagnosis an effective treatment is available. Of course, any other organ lesion found during the systemic imagery should be biopsied (especially the skin) if possible since, as in our case, this is a disseminated disease.

Given the hematopoietic malignancy nature of this disease, corticosteroids, unfortunately often given with the idea of treating a simple myelitis, generate a dramatic but transient improvement. A CHOP treatment (cyclophosphamide, doxorubicine, vincristine and prednison) is considered effective, remission exceeding 50% in some series. Methotrexate has been suggested but with less evidence and radiotherapy is recognized as ineffective. Of course, no controlled data is available because of the disease rarity.

Table 2: Suggested differential diagnosis of non traumatic conus medullaris lesion

<table>
<thead>
<tr>
<th>Condition</th>
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<tbody>
<tr>
<td>Intravascular lymphoma</td>
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<tr>
<td>Multiple sclerosis</td>
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<tr>
<td>Tuberculosis</td>
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<tr>
<td>Sarcoidosis</td>
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<tr>
<td>Endometriosis</td>
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<tr>
<td>Schistosomiasis</td>
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<tr>
<td>Cysticercosis</td>
</tr>
<tr>
<td>Toxoplasmosis</td>
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<tr>
<td>Postvaccination</td>
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<tr>
<td>Lung metastasis</td>
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</tbody>
</table>

Note: Included in this table are etiology with, to our knowledge, at least two patients reported in the literature. Differential diagnosis of cauda equina lesion is not included (e.g., HSV-2, CMV...)

Finally, we want to emphasize that when one faces the rare association of myelitis, and particularly CM syndrome, followed by encephalopathy, ILCL is potentially one of the most important entities to exclude, and should probably be considered as soon as the patient presents with a CM lesion. In the light of an effective treatment this is vital, as an early diagnosis of this otherwise lethal condition will improve the outcome.

ACKNOWLEDGEMENTS

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REFERENCES


