and Hodgkin lymphomas.\textsuperscript{3} Posttransplantation T-cell lymphomas are less common.\textsuperscript{1}

The relationship of monoclonal gammopathy to PTLD is unclear. Cutaneous extramedullary plasmacytoma was reported in cardiac transplant recipients with elevated serum immunoglobulin at diagnosis but preceding levels were not reported.\textsuperscript{4} Additionally, monoclonal gammopathy has been reported to precede the development of systemic PTLD in liver transplant recipients.\textsuperscript{5} In our patient the monoclonal protein spike was detected 3 years before clinical evidence of cutaneous PTLD.

In summary, our patient developed primary cutaneous immature plasmacytomas 10 years after renal transplantation. Evidence of EBV in the tissue helped to confirm the diagnosis of PTLD. Elevated serum immunoglobulin also supports the diagnosis of PTLD. Although PTLD in our patient resolved with radiotherapy and a decrease in immunosuppression, the patient continues under close monitoring.

\textsuperscript{CPT} Clifton R. Dabbs, DO\textsuperscript{a}
\textsuperscript{CPT} Naomi B. Creel, MD\textsuperscript{b}
LTG Stephen J. Krivda, MD\textsuperscript{b}
MAJ Daniel L. Cruser, MD\textsuperscript{c}
COL Scott A. Norton, MD\textsuperscript{b}

Departments of Internal Medicine,\textsuperscript{a} Dermatology Service,\textsuperscript{b} and Pathology\textsuperscript{c}
Walter Reed Army Medical Center
Washington, DC

The opinions or assertions contained herein are the private views of the authors and are not to be construed as official or as reflecting the views of the Department of Defense.


\textbf{REFERENCES}


\textbf{Primary carcinosarcoma of the skin}

\textit{To the Editor:} Carcinosarcoma (CS) is a biphasic tumor composed of intimately admixed epithelial and mesenchymal elements, both of which are malignant. It occurs in a variety of organs, including female and male genital tracts, lung, kidney, upper and lower urinary systems, breast, oronasopharynx, larynx, gastrointestinal tract, thyroid, thymus, and head and neck.\textsuperscript{1-4} It is extremely rare as a primary tumor in the skin; only 17 cases have been reported in the English-language literature to date.\textsuperscript{2-13} In contrast to systemic CS, cutaneous CS have a favorable prognosis with low metastatic rate and mortality. Histogenesis of these tumors remains controversial, although various hypotheses have been suggested. We describe an unusual case of

\textbf{Fig 2. A and B,} Dense nodular infiltrate of atypical plasmacytoid cells. (Hematoxylin-eosin stain; original magnifications: A, \times 20; B, \times 200.)
primary cutaneous CS that consisted of adenocarcinoma and rhabdomyosarcoma.

**CASE REPORT**

A 70-year-old woman presented with a smooth reddish exophytic mass, 2.5 cm × 2 cm × 0.5 cm, with overlying ulceration on the scalp (right temporal zone) (Fig 1). The patient reported that the lesion began as a small red papule 4 weeks earlier and had rapidly grown in size. No history of trauma in the area could be elicited. No regional lymph nodes were found to be enlarged on clinical examination. Chest radiograph and computed tomography scan of the abdomen were normal.

Histologic examination of the lesion revealed a tumor with two closely intermingled components. The epithelial tumoral component, arranged in cords and cellular nests with evidence of glandular or ductal differentiation, was a finding consistent with adenocarcinoma. The sarcomatous portion showed fascicular arrangement of atypical spindle cells with atypical rhabdomyoblasts (Fig 2). In the carcinomatous and sarcomatous components, respectively, mitotic activity was present. The tumoral stroma displayed mixed inflammatory infiltrate and variable vascular structures. Immunohistochemically the epithelial component of tumor showed epithelial membrane antigen and cytokeratin-positive immunoreactivity (Fig 3), as variable S-100 protein, whereas in the sarcomatous portion, the staining pattern was only positive for vimentin, smooth muscle actin, and desmin (Fig 4).

After complete excision of the CS, there was no evidence of disease for 1 year.

**DISCUSSION**

Malignant mixed tumors are unusual neoplasms increasingly reported in different anatomic sites. However, the histogenesis of these tumors remains unknown. Two antithetic hypotheses have been suggested to explain the histogenesis of biphasic malignant tumors. The convergence hypothesis proposes an origin from two or more undifferentiated progenitor cells (multiclonal hypothesis), and the divergence hypothesis proposes an origin from a single totipotential stem cell that differentiates into separate epithelial and mesenchymal directions (monoclonal hypothesis). One study demonstrated a monoclonal origin of systemic CS, thus, supporting the single totipotential stem cell divergence hypothesis.14
In our review of all previously reported cases (Table I), CS of the skin predominantly occurs in middle-aged and elderly persons, with an average age of 70 years and a range between 44 and 91 years of age. It affects men and women with equal frequency. Only one of the 17 patients presented with associated lymphadenopathy. Metastasis has been reported in 3 additional patients; in one of these cases was documented mortality associated to abdominal/liver metastasis. Death caused by local invasion has been reported in only one case.

The prognosis of CS of the skin is better than that of visceral areas, perhaps because of the easily detectable nature of cutaneous growth, which may prompt early diagnosis and treatment. However, long-term follow-up is needed.

Francisco Guimerá-Martín-Neda, MD
Hugo Alvarez-Arguelles, MD
Eva Facundo, PhD
Fernando Rodríguez, PhD
Rosalba Sánchez, MD
Marta García, MD
Lucio Díaz-Flores, MD
Antonio Noda, MD

Departments of Dermatology and Pathology
Hospital Universitario de Canarias
University of La Laguna
Tenerife (Canary Islands), Spain

Correspondence to:
Francisco Guimerá-Martín-Neda, MD
C/San Vicente Ferrer, nº 61, piso 2º, pta. 10
38002 - Santa Cruz de Tenerife (Canary Islands), Spain
E-mail: fjguimera@hotmail.com

REFERENCES

Table I. Previously reported cases of primary cutaneous carcinosarcomas

<table>
<thead>
<tr>
<th>Case no.</th>
<th>Age (y)/sex</th>
<th>Site</th>
<th>Malignant epithelial component</th>
<th>Malignant mesenchymal component</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Dawson⁵</td>
<td>75/M</td>
<td>Chest wall</td>
<td>Basal cell/squamous cell Ca</td>
<td>Chondroid, osteoid</td>
</tr>
<tr>
<td>2. Quay et al⁶</td>
<td>74/M</td>
<td>Axilla</td>
<td>Basal cell Ca</td>
<td>Chondroid, osteoid</td>
</tr>
<tr>
<td>3. Iakovides et al⁸</td>
<td>72/M</td>
<td>Upper aspect of arm</td>
<td>Squamous cell Ca</td>
<td>Fibrous histiocytes</td>
</tr>
<tr>
<td>4. Iakovides et al⁸</td>
<td>69/F</td>
<td>Forearm</td>
<td>Squamous cell Ca</td>
<td>Fibrous histiocytes</td>
</tr>
<tr>
<td>5. Tschen et al⁷</td>
<td>91/F</td>
<td>Forehead</td>
<td>Basal cell Ca</td>
<td>Osteoid, osteoelasticite</td>
</tr>
<tr>
<td>6. McKee et al⁹</td>
<td>52/F</td>
<td>Iliac crest</td>
<td>Malignant spiradenoma</td>
<td>Osteoid, chondroid</td>
</tr>
<tr>
<td>7. McKee et al⁹</td>
<td>45/F</td>
<td>Upper aspect of arm</td>
<td>Malignant spiradenoma</td>
<td>Osteoid, osteoelasticite</td>
</tr>
<tr>
<td>8. Izaki et al¹⁰</td>
<td>44/M</td>
<td>Back</td>
<td>Basal cell Ca</td>
<td>Spindle cells</td>
</tr>
<tr>
<td>9. Hanly et al¹¹</td>
<td>36/M</td>
<td>Face</td>
<td>Pilomatrixoma</td>
<td>Spindle cells</td>
</tr>
<tr>
<td>10. Leen et al¹²</td>
<td>86/M</td>
<td>Face</td>
<td>Basal cell/squamous cell Ca</td>
<td>Osteoid, spindle cells</td>
</tr>
<tr>
<td>11. Biernat et al²</td>
<td>69/F</td>
<td>Upper aspect of arm</td>
<td>Squamous cell Ca</td>
<td>Spindle cells</td>
</tr>
<tr>
<td>12. Patel et al³</td>
<td>71/M</td>
<td>Eyelid</td>
<td>Squamous cell Ca</td>
<td>Osteoid</td>
</tr>
<tr>
<td>13. Patel et al³</td>
<td>74/M</td>
<td>Scalp</td>
<td>Squamous cell Ca</td>
<td>Smooth/skeletal muscle</td>
</tr>
<tr>
<td>14. Patel et al³</td>
<td>83/M</td>
<td>Head</td>
<td>Squamous cell Ca</td>
<td>Osteoid, chondroid</td>
</tr>
<tr>
<td>15. Patel et al³</td>
<td>64/M</td>
<td>Nose</td>
<td>Eccrine poro-Ca</td>
<td>Osteoid, osteoelasticite</td>
</tr>
<tr>
<td>16. Brown et al⁴</td>
<td>72/M</td>
<td>Upper aspect of arm</td>
<td>Basal cell Ca</td>
<td>Spindle cells</td>
</tr>
<tr>
<td>17. Inaloz et al³</td>
<td>73/F</td>
<td>Forearm</td>
<td>Basal cell Ca</td>
<td>Spindle cells</td>
</tr>
<tr>
<td>18. Current case</td>
<td>70/F</td>
<td>Scalp</td>
<td>Adeno-Ca cells</td>
<td>Skeletal muscle, spindle cells</td>
</tr>
</tbody>
</table>

Ca, Carcinoma; F, female; M, male.
Ampicillin-induced cutaneous eruption associated with Epstein-Barr virus reactivation

To the Editor: Cutaneous eruption associated with ampicillin use in patients with infectious mononucleosis (IM) and Epstein-Barr virus (EBV) primary infection are well established. The interaction between viral infections and antibiotic exposure resulting in cutaneous eruption is not clearly understood. Here we report a case of ampicillin-induced eruption associated with EBV reactivation. To our knowledge, this is the first report of drug eruption related to EBV reactivation.

A 23-year-old woman diagnosed with adult-onset Still’s disease based on diagnostic criteria such as evanescent erythematous-edematous cutaneous eruption, fever, neutrophilia, hepatic dysfunction, and absence of autoantibodies including rheumatoid factor, was treated with prednisolone (40 mg/day) and ampicillin (1000 mg/day). Although the features of Still’s disease were improved, the erythematous macular and papular skin lesions appeared 7 days after treatment (Fig 1, a and b). Under suspicion of drug-induced eruption, ampicillin was stopped and the rash gradually disappeared. One week after the onset of cutaneous eruption, serum IgG antibody titer to EBV-VCA was 1:640. She had no history of IM.

Challenge test with intravenous ampicillin (100 mg) was performed 39 days after the first medication with ampicillin. Cutaneous eruption was induced on the face, trunk, and limbs in 24 hours after the challenge. According to previous reports that ampicillin did not induce cutaneous eruption after recovery from IM, the second challenge test was performed after recovery from active EBV infection (90 days after first medication with ampicillin). Cutaneous eruption was also induced on the whole body (Fig 1, c and d). To eliminate the possibility that oral prednisolone had an influence on EBV-DNA levels, a third challenge test was performed 11 days after stopping treatment with oral prednisolone (165 days after first medication with ampicillin), and the same result was observed.

We tried to monitor the concentration of EBV-DNA in the blood samples obtained from the patient at different time points with or without cutaneous eruption (Fig 2). EBV-DNA concentrations in the peripheral blood mononuclear cells of each blood sample were measured using real-time polymerase chain reaction analysis. A high level of EBV-DNA was detected at the time of the first appearance of macular and papular rash. Furthermore, a high level of EBV-DNA was observed 24 to 48 hours after every challenge test just before the appearance of cutaneous eruption (60-270 copies/μg DNA). EBV-DNA was detected in CD19-positive cells (B cells), while there was no EBV-DNA detected in CD19-negative cells.

The characteristic features in this patient were erythematous macular and papular cutaneous eruption with EBV reactivation after the initial administration and subsequent challenges with ampicillin. Although the mechanism of EBV reactivation by ampicillin is still unknown, drug-induced viral