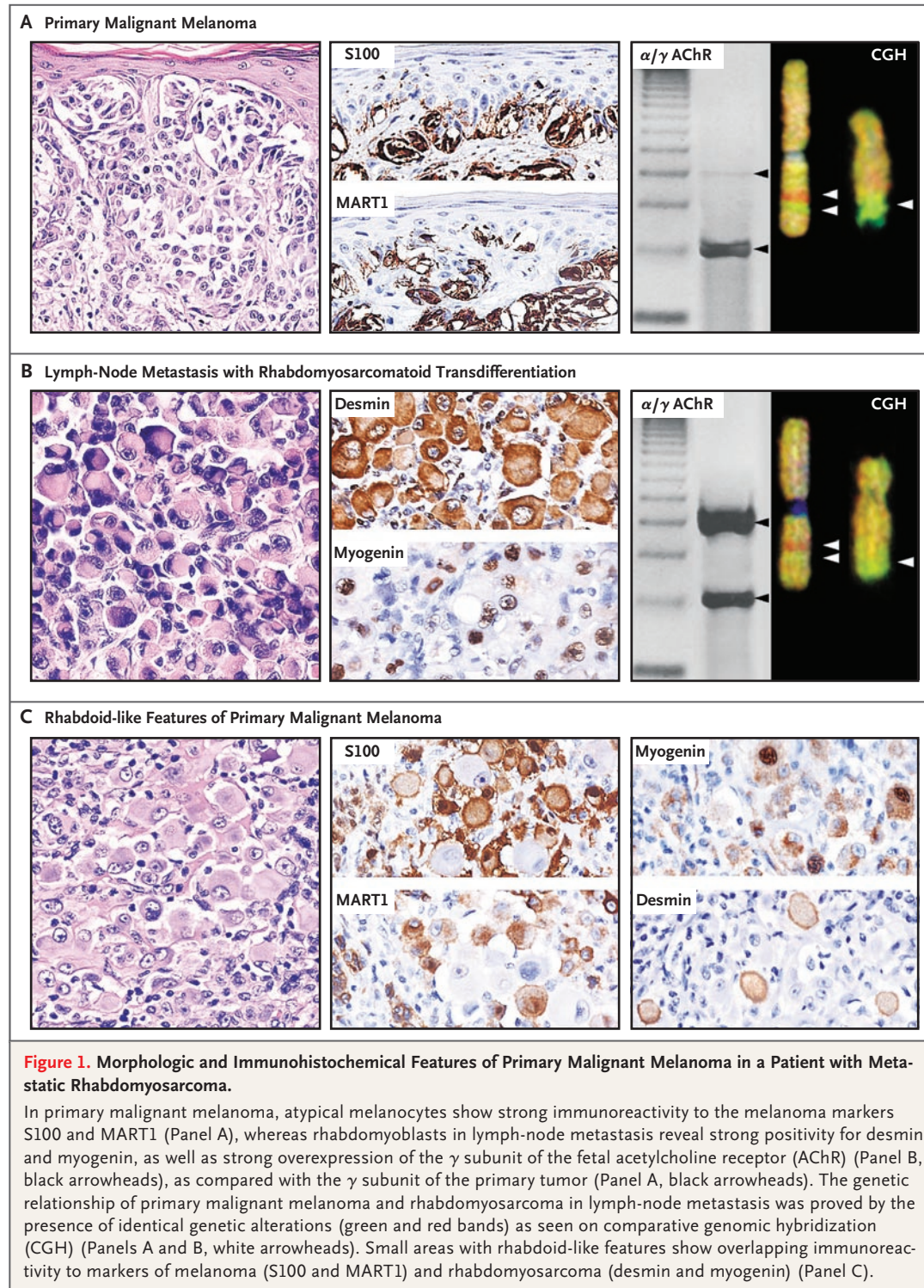


# Malignant Melanoma with Metastatic Rhabdomyosarcomatoid Transdifferentiation

**TO THE EDITOR:** We report on the case of a 41-year-old man with a 2.1-cm primary malignant melanoma of the skin, located on the crown of the head. The tumor was stage pT4 (with invasion of contiguous structures), Clark level V, and 6 mm in thickness, with classic morphologic and immunohisto-



chemical features, including strong positivity for the malignant melanoma-specific immunomarkers S100 and MART1 (Fig. 1A).

Three months after complete resection of the tumor, multiple enlarged cervical lymph nodes developed, with the complete morphologic and immunohistochemical phenotype of a rhabdomyosarcoma, including characteristic rhabdomyoblasts that were strongly positive for desmin and myogenin and up-regulation of fetal acetylcholine receptor; the latter was shown to be specific for rhabdomyosarcoma<sup>1</sup> (Fig. 1B). In serial sections of the primary tumor, we found small nests of rhabdomyoblasts with overlapping immunoreactivity for both melanoma and rhabdomyosarcoma markers (Fig. 1C), in addition to shared genetic alterations (loss of chromosome 1q31, amplification of 1q32, and gain of 12q23-qter), which were detected with the use of comparative genomic hybridization (Fig. 1A and 1B).

In spite of intensive radiochemotherapy (56 Gy of cobalt-60 gamma rays and one cycle of dacarbazine [DITC]), the patient died from generalized spread of rhabdomyosarcoma 6 months after primary diagnosis. The metastases involved the lung, mediastinum, and abdominal organs with malignant ascites.

In previous studies of primary and metastatic melanoma with rhabdoidlike features,<sup>2</sup> neither the morphologic nor the genetic relationship of a primary melanoma with a rhabdoid transdifferentiation in metastasis could be demonstrated. In our patient, the primary lesion had intratumorous rhabdoidlike features and subsequent complete metastatic rhabdomyosarcomatoid transdifferentiation, as shown by morphologic and immunohistochemical analysis and comparative genomic hybridization.

Although the genetic pathways involved in such transdifferentiation still remain unknown, the expression of the mesenchymal and neuroectoder-

mal stem-cell markers CD166, CD133, and nestin<sup>3</sup> and of melanoma inhibitory activity (MIA) protein<sup>4</sup> on differentiating human mesenchymal stem cells highlights the mesenchymal and myogenic potential of melanoma stem cells. These interactions may be a part of the genetic program that is responsible for rhabdoid transdifferentiation in malignant melanoma.

Moreover, since the rhabdoid phenotype is highly associated with a poor prognosis, and since neoplasms with complete rhabdomyosarcomatoid transdifferentiation are not responsive to conventional chemotherapy,<sup>5</sup> alternative treatments for these advanced-stage diseases must be considered. Such therapies could include immunotherapeutic regimens with the use of chimeric T cells or immunotoxins that target the fetal acetylcholine receptor.<sup>1</sup>

Stefan Gattenlöhner, M.D.

Eva-Bettina Brocker, M.D.

Hans-Konrad Muller-Hermelink, M.D.

University of Würzburg

97080 Würzburg, Germany

stefan.gattenloehner@mail.uni-wuerzburg.de

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