A man in his 30s presented with a 7-cm left renal mass for which he underwent a radical nephrectomy. Histopathologic examination revealed a neoplasm predominantly composed of spindled cells (Figure 1A, magnification ×40). On higher magnification, these cells had a relatively bland appearance with minimal cytologic atypia and mitotic activity (Figure 1B, magnification ×200). Focal areas of this tumor (<5%) had a tubular component with extravasated mucin (Figure 1C, magnification ×100). Immunohistochemistry showed expression of the transcription factor PAX8 (Figure 1D, magnification ×200) as well as keratin 7 in both the epithelial and spindle cell component. Diagnostic markers of other common mesenchymal neoplasms of the kidney that are typically composed of bland spindle cell proliferations were absent (HMB45, Melan-A, smooth muscle actin). This immunophenotype excluded mesenchymal neoplasms such as angiomyolipoma and leiomyoma.

Based on the presence of focal biphasic features, the immunophenotype, and the cytogenic profile, the tumor was diagnosed as a mucinous tubular and spindle cell carcinoma.
Which of the following cytogenetic profiles supports a diagnosis of mucinous tubular and spindle cell carcinoma of the kidney?

a. Gains of chromosome 7 and 17  
b. Loss of the short arm of chromosome 3  
c. Multiple losses of chromosomes 1, 4, 6, 8, 9, 13, 14, 15, and 22  
d. Homozygous deletion of the CDKN2A/B gene region

Answer: c. Multiple losses of chromosomes 1, 4, 6, 8, 9, 13, 14, 15, and 22.

A single-nucleotide polymorphism—based microarray revealed the presence of multiple chromosome losses, including chromosomes 1, 3, 4, 6, 8, 9, 10, 13, 14, 15, 16, 21, 22, and Y. Other findings included a gain of chromosome 18 and copy neutral loss of heterozygosity of chromosomes 2 and 7. These findings are depicted in Figure 2, with relative (log2) ratios on the y-axis and corresponding chromosomes being listed on the x-axis. As a characteristic pattern of chromosome losses (1, 4, 6, 8, 9, 13, 14, 15, and 22) has been reported in mucinous tubular and spindle cell carcinoma of the kidney, this cytogenetic profile supported this diagnosis. Many of the immunohistochemistry-based markers that are commonly used in the characterization of renal tumors lack specificity in establishing this diagnosis. Other biomarkers that have been described for this tumor include VSTM2A, which can be detected using RNA in situ hybridization.

Several kidney tumors have specific patterns of unique and recurrent cytogenetic alterations, including gains of chromosome 7 and 17 in papillary renal cell carcinoma and loss of chromosome 3p in clear cell renal cell carcinoma. In some studies of locally advanced/metastatic mucinous tubular and spindle cell carcinoma of the kidney, the reported spectrum of additional cytogenetic alterations included a gain of chromosome 1q or homozygous deletion of the CDKN2A/B gene region, neither of which was identified in this tumor. In summary, cytogenetic profiling using a single-nucleotide polymorphism—based microarray helped in the diagnosis of this tumor.

REFERENCES