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INTRODUCTION

A significant proportion of renal cell carcinomas (RCC) of children and young adults bear specific chromosome translocations resulting in gene fusions that involve members of the MiTF/TFE transcription factor family. These include the Xp11.2-translocation carcinomas, which bear TFE3 gene fusions, and the renal carcinomas with the t(6;11)(p21;q12), which bear an Alpha-TFEB gene fusion (1).

The Xp11.2-translocation tumors themselves include two variants, namely one with t(X;1)(p11.2;q21) resul-

Xp11 translocation carcinoma of the kidney presenting with Multilocular cystic renal cell carcinoma-like features

Presentamos el caso de una joven de 17 años con un tumor multiquístico en la parte media del riñón derecho. Una nefrectomía parcial mostró un tumor epitelial con un patrón de Carcinoma de células renales multiquístico, con células que revelaron fuerte reacción nuclear para la proteína TFE3, apoyando el diagnóstico de Carcinoma renal con translocación Xp11. No hemos podido hallar un caso similar en la literatura. El caso subraya la necesidad de plantearse varios diagnósticos diferenciales para realizar el diagnóstico certero de las variedades de carcinoma renal.

Palabras clave: carcinoma de células renales; carcinoma renal con translocación Xp11; TFE3; tumores renales

We are reporting the case of 17 year-old-female with a multicystic tumor in the middle of the right kidney. Partial nephrectomy revealed an epithelial tumor with multilocular cystic renal cell carcinoma pattern, with the cells exhibiting strong nuclear reactivity for TFE3 protein, supporting the diagnosis of Xp11 translocation carcinoma of the kidney. We have not been able to find a similar case in the literature. The case emphasizes the high index of suspicion needed for accurate diagnosis of renal carcinomas.

Keywords: kidney tumor; renal cell carcinoma; TFE3; Xp11 translocation carcinoma.

ting in PRCC-TFE3 gene fusion (2), and another with balanced t(X;17)(p11.2;q25) presenting ASPL-TFE3 fusion transcripts (3,4). The gross and microscopic features of the Xp11.2-translocation tumors are difficult to assess since there are still not too many cases reported. For the former the predominant histologic pattern is reported as nests of epithelial cells, with islands of tumor cells compartmentalized by thin-walled capillary vasculature. Minor variations on this pattern include solid, acinar, alveolar, and tubular architecture. Papillary architecture may be present, usually as a minor component. Neoplastic cells are typically characterized by irregularly shaped nuclei with vesicular chromatin and small nucleoli not

visible with a 10x objective, and cytoplasm that ranges from clear to densely granular and eosinophilic. As for the t(X;17) cases the histology is reported as demonstrating nested and pseudopapillary patterns of growth, psammomatous calcifications, and epithelioid cells with abundant clear cytoplasm and well-defined cell borders. The immunohistochemistry of both shows the expression of TFE3 in the nuclei of cells (2-5).

Cystic degeneration is not uncommon in renal cell carcinoma. In a review of the AFIP experience, Hartman et al found that 15 % of all renal cell carcinomas in their files were cystic (6). For the most part "cystic RCC" does not represent a specific entity but rather reflects a degenerative or unusual growth pattern in a tumor belonging to one of the recognized subtypes of RCC (7). One specific cystic tumor, Multilocular Cystic Renal Cell Carcinoma (MCRCC) has been included in current classifications as a subtype of clear cell RCC (8, 9).

MCRCC has been considered a distinct subtype of clear cell RCC by the recent 2004 WHO classification based on the characteristic gross and microscopic features (10). In the literature, no tumor with these features has ever recurred or metastasized (11). On the largest series of MCRCC in the English literature incorporating the recent 2004 WHO diagnostic criteria published 11 100 % patients were alive without evidence of disease at a mean follow-up of 66.1 months. MCRCC occurs slightly more often in men than in women (1.7:1), but women had tumors at an earlier age (mean age 51.1 years; range 36 to 80 years) than men (mean age 56.3 years; range 30 to 78 years). Low Fuhrman grade and stage are characteristic features of MCRCC with only rare cases having stage T3 (11). Most reported cases of MCRCC were NOM0 at diagnosis further suggesting a low malignant potential tumor (11).

Present report describes a peculiar gross and microscopic presentation of an Xp11 translocation carcinoma of the kidney, namely a MCRCC-like pattern.

CASE REPORT

A 17 year-old-female presented with bilateral lumbar pain, more intense to the right side. Ultrasound examination revealed a solid non-homogeneous, 3 cm mass in the middle of the right kidney. A CT scan showed the lesion (Figures 1-2) to be a complex mostly cystic mass, 2.4 cm in diameter (Bosniak III).

A partial nephrectomy was performed as enucleation of a cystic lesion (nephron-sparing surgery). Postoperative course was uneventful and after approximately at 4 months of follow-up the patient is alive and well.

Pathology examination showed a piece of kidney measuring 4.2 x 3.6 x 1.6 cm presenting in the middle portion an almost black, cystic, circumscribed mass, of 2.1 x 1.6 cm (Figure 3). The cross-section revealed a multicystic well-delimited lesion (Figure 4), measuring 3.5 cm, that was subdivided by thin membranous and fibrous septa into variously sized round or oval cavities. The septa contained some small yellow nodules. The cysts were filled with serous fluid. No invasion of the capsule or residual normal renal parenchyma was evident.

Microscopic examination of H&E stained sections allowed to recognize that the mass was well delimited by fibrous tissue. The cysts walls and septa (Figure 5) were lined for the most part by a single layer of clear cells with grade 3 nuclear atypia (Figure 6). These cells were columnar, cuboidal or flattened. The intercystic septa were thin, fibrous, and contained a few sheets of clear tumor cells (Figure 7) also with grade 3 nuclear atypia. A great number of psammoma bodies were found (Figure 8). Small papillary structures were present (Figure 9). Many foci of entrapped smooth muscle tissue were present in the septa (Figure 10). The cavities of the cysts either contained homogeneous proteinaceous material or appeared to be empty.

Immunohistochemical analysis for the TFE3 protein showed strong nuclear labeling in the tumor cells (Figures 11-12).

Based in these findings the tumor was diagnosed as a Xp11 translocation carcinoma of the kidney presenting with Multilocular cystic renal cell carcinoma-like features, nuclear grade 3 (according to the Fuhrman grading system) and classified as pT1aNXMXG3 (according to the TNM system 2002), stage I.

DISCUSSION

Small areas with papillary pattern, presence of psammoma bodies, high nuclear grade, and age of the patient all supported the possibility that this multicystic tumor represented an example of Xp11 translocation carcinoma (1-5). However, as referred above the gross and certainly

certain microscopic features made this lesion quite reminiscent of the MCRCC.

Present report widens the spectrum of gross and microscopic features to be found in Xp11 translocation carcinoma. Due to the already known aggressive behavior of this tumor the patient is under close follow-up.

ACKNOWLEDGMENTS

We thank the Dept. of Pathology, John Hopkins Hospital, Baltimore, MD, USA, for the H&E and TFE3 immuno-histochemical stains.

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ICONOGRAFÍA

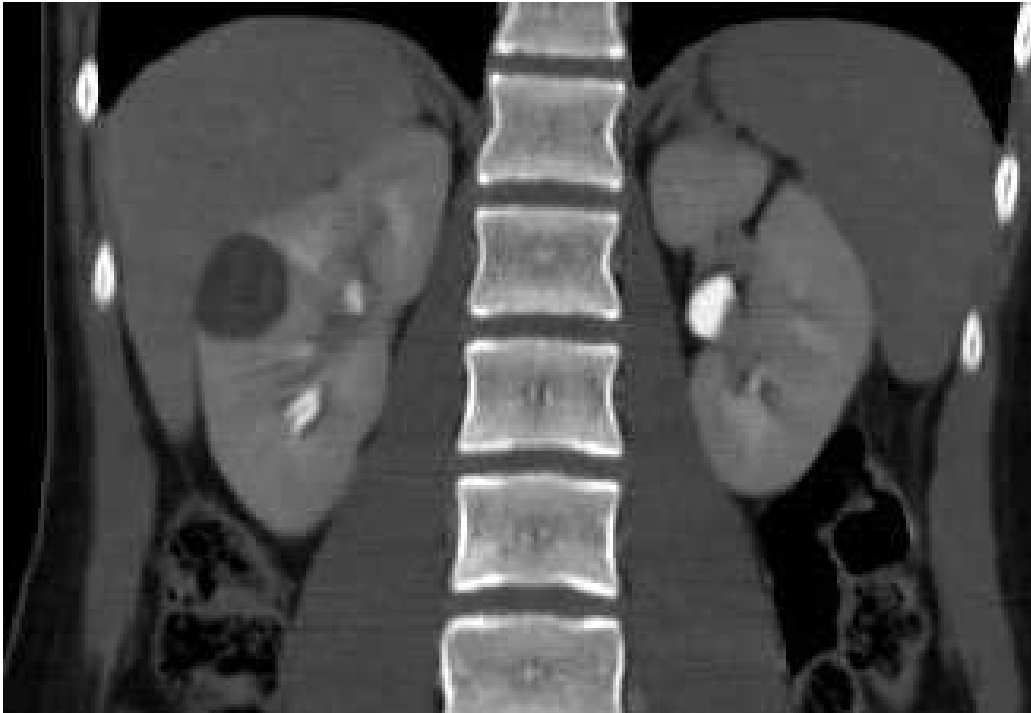


Figure 1.- Axial CT image shows a complex cystic mass in the middle portion of the right kidney.

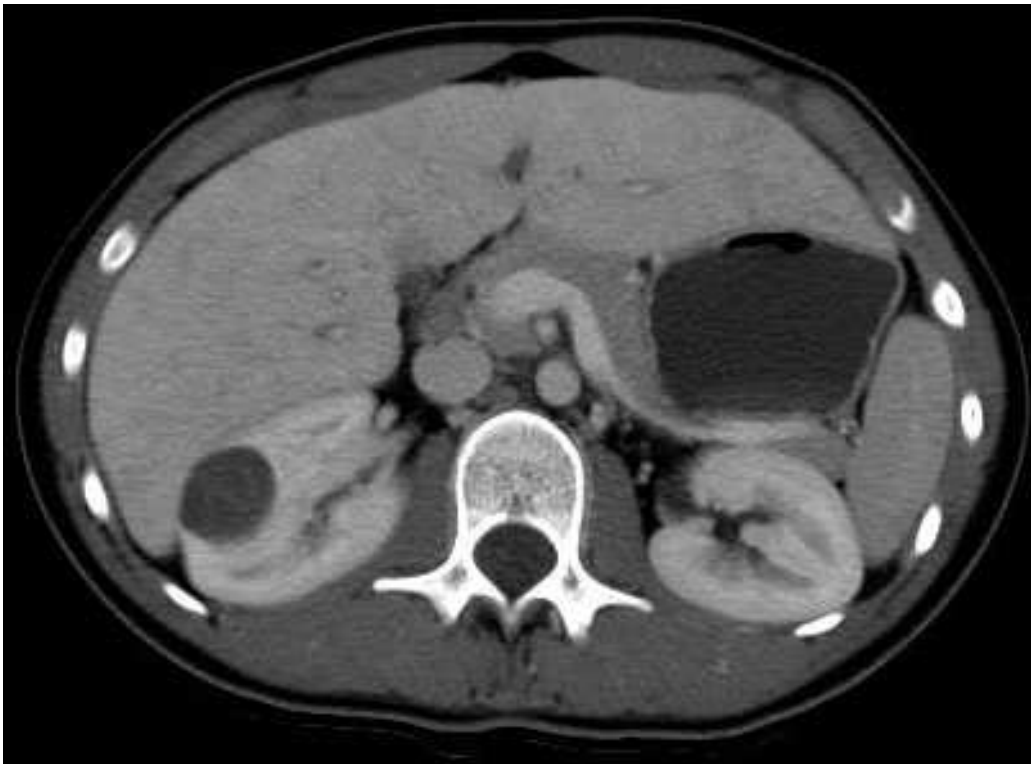


Figure 2.- Coronal reconstruction showing that the mass has no relation with the pelvicalyceal system.



Figure 3.- Macroscopic examination, showing a central, black, cystic, well circumscribed renal mass.



Figure 4.- Macroscopic examination in cross-section, showing multicystic well-delimited kidney lesion.

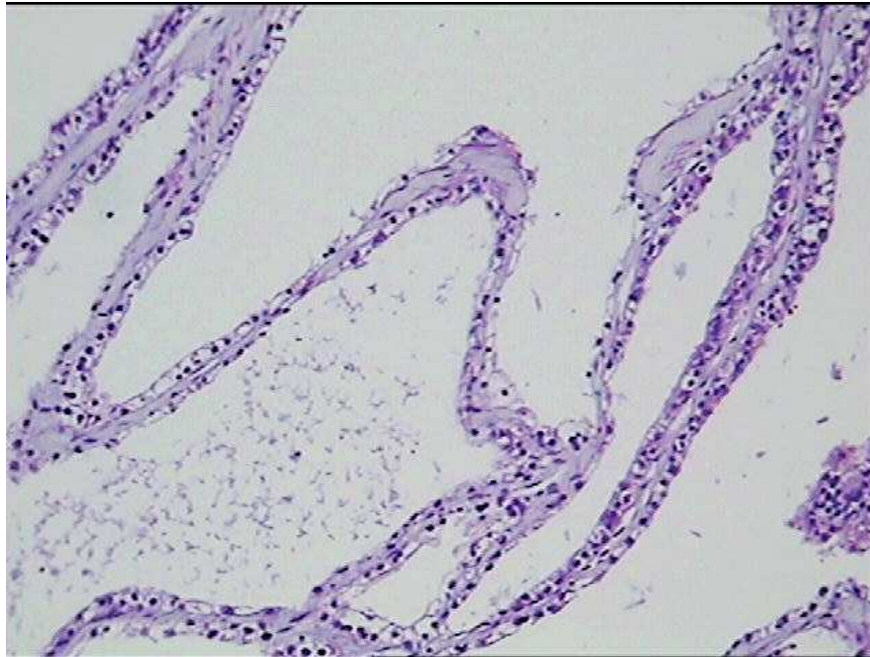


Figure 5.- Intermediate-power view of the case showing thin membranous and fibrous septa (H&E, original magnification, x100).



Figure 6.- High-power view of the case showing septa lined for clear cells (H&E, original magnification, x400).

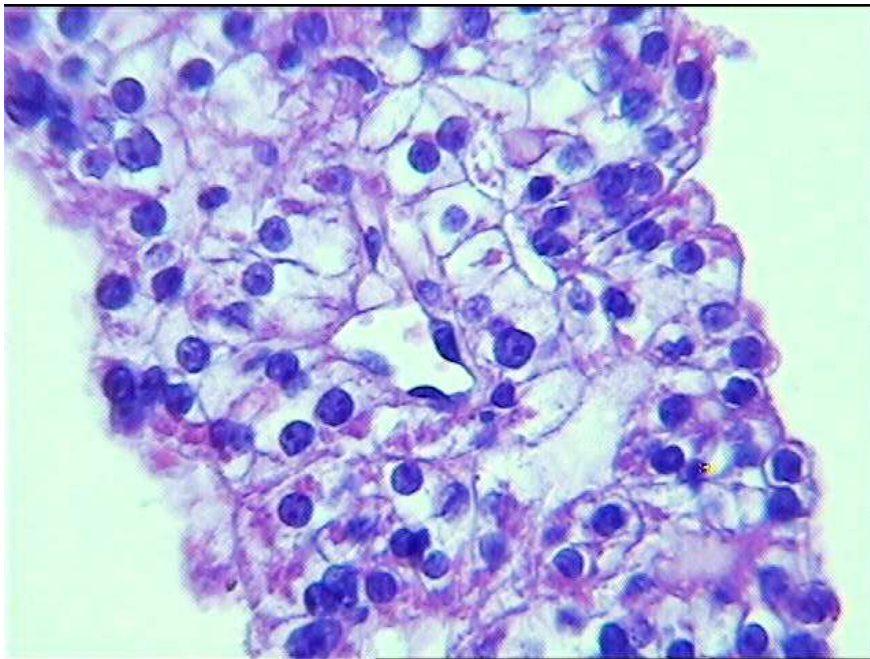


Figure 7.- High-power view of the case showing clear tumor cells in the septa (H&E, original magnification, x400).

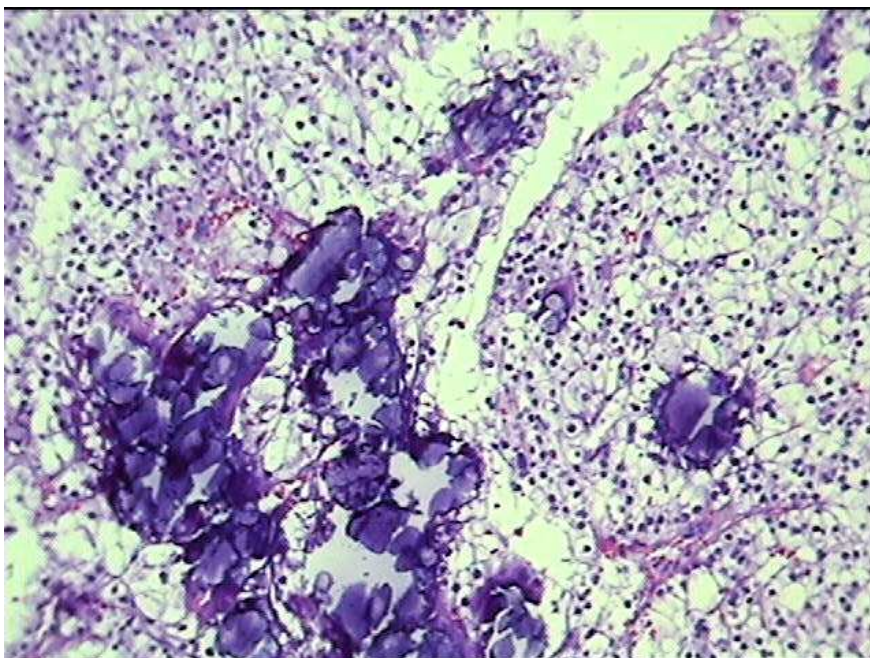


Figure 8.- Intermediate-power view of the case showing psammoma bodies (H&E, original magnification, x100).

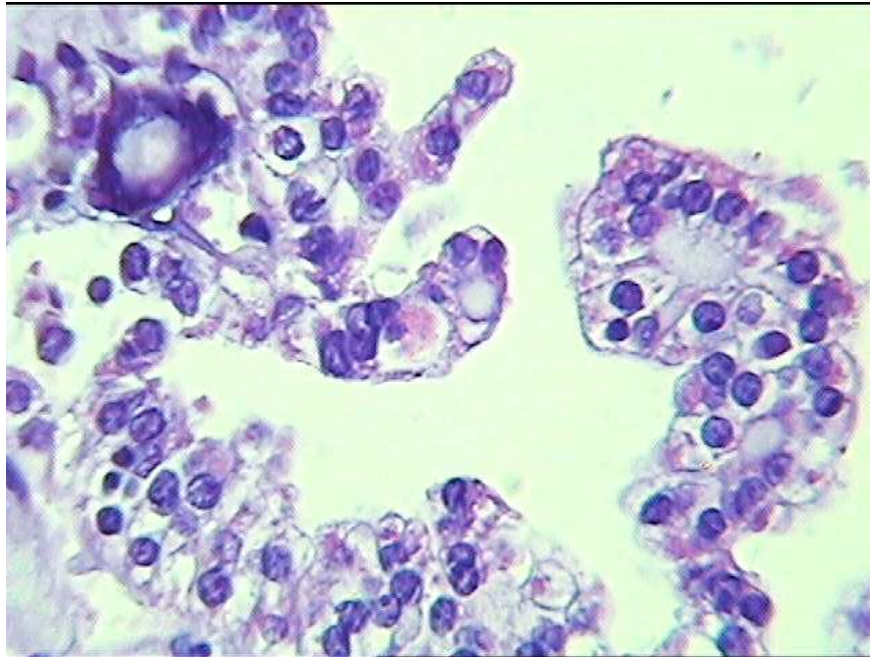


Figure 9.- High-power view of the case showing small papillary structures (H&E, original magnification, x400).

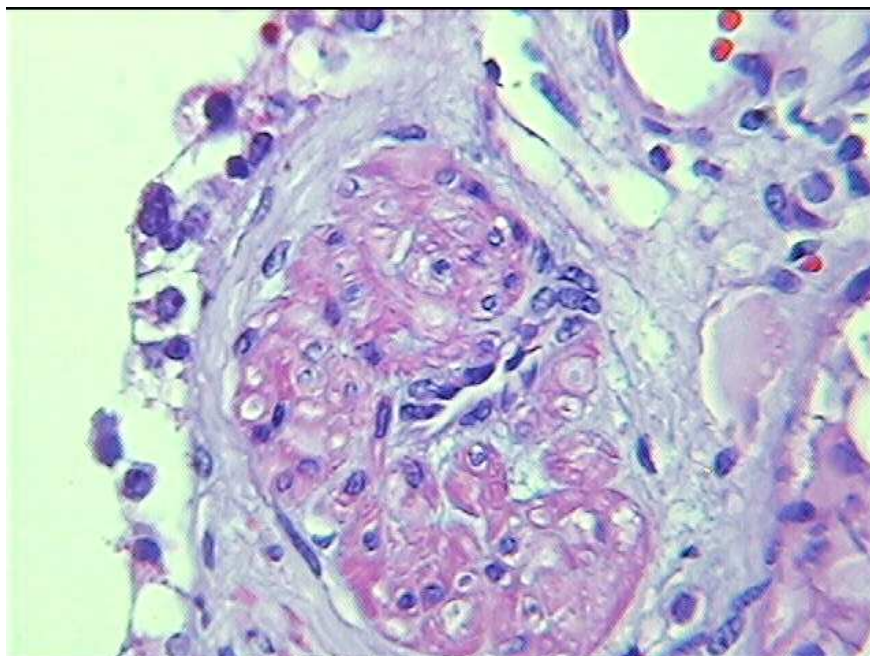


Figura 10.- High-power view of the case showing a smooth muscle island in the septa (H&E, original magnification, x400).

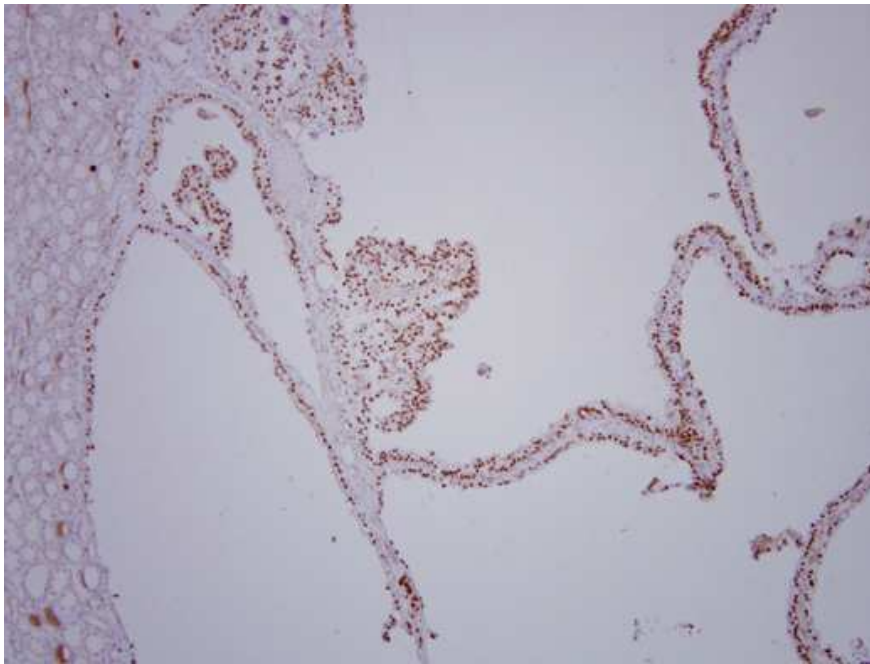


Figura 11.- Intermediate-power view of the case showing strong nuclear labeling in the tumor cells (TFE3, original magnification, x100).

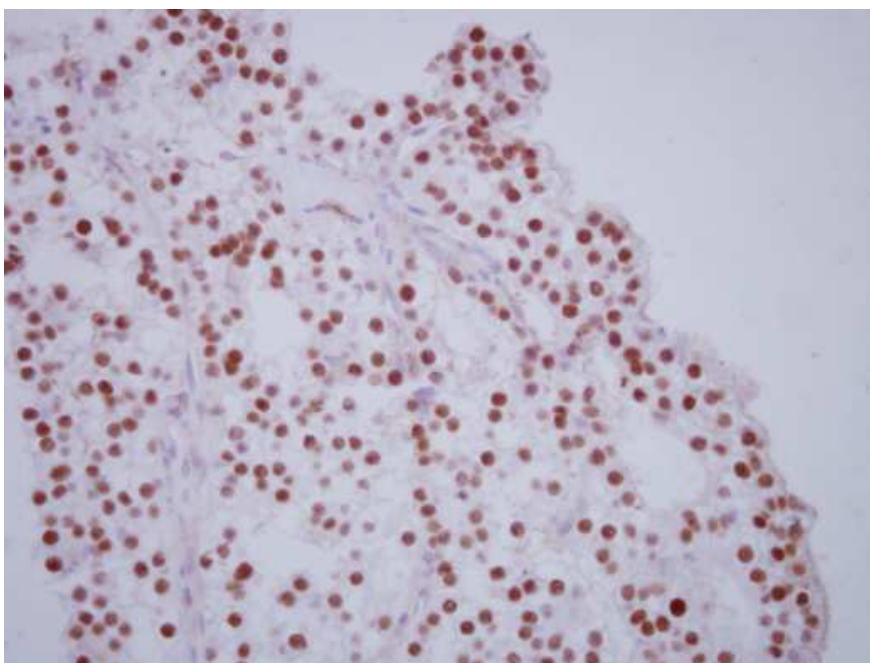


Figura 12.- High-power view of the case showing strong nuclear labeling in the tumor cells (TFE3, original magnification, x400).