Case Report

Is the presence of IgG4+ cells within urothelial carcinomas of the renal pelvis that contain rhabdoid and sarcomatoid features associated with IgG4-related diseases?

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Abstract: A 69-year-old male underwent nephrectomy after presenting with a renal mass, as visualized through imaging. Histologic evaluation of the specimen revealed a papillary urothelial carcinoma (UC) in the renal pelvis with infiltration into the renal parenchyma that showed sarcomatoid and rhabdoid features; these features are typically associated with mixed inflammatory infiltrate, storiform fibrosis, and obliterative phlebitis, which is reminiscent of IgG4-related disease (IgG4-RD). Immunohistochemical labeling for IgG4 plasma cells showed that there were >50 cells in a single high-power field and the ratio of IgG4/IgG was >40%; these results are consistent with a diagnosis of IgG4-RD. Herein, we describe the first case of UC that has both sarcomatoid and rhabdoid features and high proportions of IgG4+ plasma cells.

Keywords: IgG4, plasma cell, urothelial carcinoma, rhabdoid

Introduction

Urothelial carcinomas (UCs) can, in rare cases, present with rhabdoid features. Less than 20 cases have been reported to date [1-5]. The prognosis of UC with rhabdoid features is poor and such cases are typically characterized by an aggressive clinical course [4, 6]. Even though most such cases have conventional UC features, at least focally, sometimes they are diagnostically challenging [6]. In UC cases with rhabdoid features, various coexistent histologic components were also found, including urothelial carcinoma in situ, high-grade UC, poorly differentiated carcinomas with small-cell features, and sarcomatoid components [2, 4].

Many types of carcinomas can be associated with IgG4+ plasma cells, independent of whether IgG4-related disease (IgG4-RD) is present. However, this is the first case report to describe a case of UC associated with IgG4+ plasma cells. In this report, we describe the clinico-pathologic characteristics of a case of UC with rhabdoid and sarcomatoid features that is also accompanied by an inflammatory myofibroblastic tumor-like area enriched with IgG4+ plasma cells.

Case report

The patient was a 69-year-old male who had had macroscopic hematuria for 5 months. Imaging modalities, including CT and MR revealed a 3.5-cm mass in the lower pole of the right kidney. Selective urine cytology on the right ureter showed atypical urothelial cells. A transurethral cystoscopic examination found no mass lesions in the urinary bladder. Thus, a nephrectomy was performed, which revealed, through gross observation a papillary mass in the renal pelvis. In the cross-sectional view, a tumor infiltrating the renal parenchyma was observed (Figure 1A). In the scanning view, the tumor appeared to be heterogeneous and hemorrhage and necrosis were visible (Figure 1B). With a higher resolution focus, prominent sarcomatoid and rhabdoid features with inflammatory cells in the renal parenchyma were observable (Figure 1C) and geographic zonal necrosis.
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was focally present (Figure 1D). The carcinoma extended to the renal capsule without penetration and the papillary tumor in the renal pelvis showed a typical papillary urothelial carcinoma (Figure 2B).

Characteristic rhabdoid tumor cells are large and oval or round with a thick eosinophilic cytoplasm and eccentric nuclei with a hyperchromatic or vesicular appearance (Figure 2C). The rhabdoid cells were singly scattered within the sarcomatoid area (Figure 2D), and made up approximately 20-30% of the total tumor volume. The renal parenchyma was remarkable because of its dense inflammatory cell infiltration. The inflammatory infiltrate was mainly composed of lymphoplasma cells with many eosinophils. Scattered lymphoid follicles were present in the peritumoral area. Obliterative phlebitis was identified (Figure 3A) and perineural plasmacytic infiltration was noted in some areas. Inflammatory infiltration was closely associated with storiform fibrosis (Figure 3B).

Based on immunohistochemical studies, tumor cells were positive for panCK, vimentin, EMA, and INI-1, but negative for S-100, p63, and GATA-3. Focal areas show large numbers of IgG4-expressing plasma cells (Figure 3D) with >50 cells per one high power field. The ratio of IgG4/IgG was >40% (Figure 3C). Data on IgG4 serum levels were not available for this patient, but there was no evidence of IgG4 systemic disease. The patient received systemic chemotherapy and, 6 months later, is still alive without tumor recurrence or metastasis.

Discussion

In this report, we describe a case of urothelial carcinoma (UC) with rhabdoid and sarcomatoid features accompanied by heavy IgG4+ plasma...
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Cell infiltration and storiform fibrosis, reminiscent of inflammatory myofibroblastic tumors or IgG4-related disease (IgG4-RD).

UCs have a wide histologic spectrum of differentiation. However, only a few UC cases with rhabdoid features have been reported in the literature [1-5]. The clinical behaviors of these cancers are not well understood, but they are generally thought to have poor outcomes. According to a report of 6 cases, UCs with rhabdoid features can coexist with multiple histologic components, including in situ urothelial carcinoma, high-grade urothelial carcinoma, and poorly differentiated carcinoma with small-cell features, sarcomatoid and myxoid components [4]. Intriguingly, among their 6 cases, three had areas that mimicked inflammatory myofibroblastic tumors; however, their association with IgG4-RD was not explored [4].

IgG4-RD is characterized by enlargement of the affected organs along with elevated levels of serum IgG4, abundant infiltration of IgG4-bearing plasma cells and fibrosis [7]. The condition was first described in relation to the pancreas and is now called type 1 autoimmune pancreatitis (AIP) [8]. IgG4-RD with pancreatic cancer has been reported in patients with AIP [9, 10]. Besides pancreatic cancer, IgG4+ plasma cell infiltration can also be found in many cancers, but their clinical relevance for IgG4-RD has not yet been demonstrated. In one study, malignancies occurred in 10.4% of IgG4-RD patients, which is approximately 3.5 times higher than the incidence of cancer in the general population [11]. Large numbers of IgG4+ plasma cells are ubiquitous in diverse localized non-specific chronic inflammatory conditions, as well as in primary cancers, therefore, IgG4+ plasma cell counts or IgG4/IgG ratios do not

Figure 2. Microscopic features of urothelial carcinoma with rhabdoid and sarcomatoid differentiation: A. Scanning image. B. High-power image of the papillary tumor revealed a typical papillary urothelial carcinoma (HE, ×100). C. Rhabdoid cells were large and oval to round with abundant eosinophilic cytoplasm and eccentric nuclei with nucleoli (HE, ×200). D. The sarcomatoid area with scattered rhabdoid cells and inflammatory cells: an atypical mitotic figure is noted (arrow) (HE, ×200).
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reliably distinguish IgG4-RD from non-specific chronic inflammation, per se [12]. At the 2011 international symposium on IgG4-RD (Boston, Massachusetts), a proposal for pathologic diagnoses of IgG4-RD was suggested [7]. A diagnosis of IgG4-RD requires the combined presence of a characteristic histopathologic appearance and elevated numbers of IgG4+ plasma cells. The critical pathologic features include dense lymphoplasmacytic infiltrate, storiform fibrosis patterns, and obliterative phlebitis. In this case, we observed a focal storiform fibrosis pattern, dense lymphoplasmacytic infiltrate with increased eosinophils, and IgG4+ plasma cells.

It remains uncertain whether this case is a UC with secondary intratumoral and peritumoral inflammatory responses that are characteristic of increased fibrosis and IgG4+ plasma cells or a UC that developed as a complication of IgG4-RD. Recently, IgG4-related kidney disease (IgG4-RKD) has been proposed as a comprehensive term for all renal lesions associated with IgG4-RD [13]. The most dominant features of IgG4-RKD are fibrosis and plasma-cell-rich tubulointerstitial nephritis with increased IgG4+ plasma cells [14]. The conclusion that this UC case is a complication of IgG4-RD is unlikely because non-neoplastic kidney tissue did not show typical histologic features of IgG4-RKD, suggesting that the cancer may have caused the secondary inflammatory response. The risk of genitourinary tract malignancies associated with IgG4-RD is unknown; only three renal cell carcinomas associated with autoimmune pancreatitis have been reported [15].

In conclusion, rhabdoid differentiation of UC is extremely rare, but may coexist with multiple histologic features, including an inflammatory myofibroblastic tumor-like area that may also have IgG4+ plasma cells and fibrosis, resembling IgG4-RD.
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Disclosure of conflict of interest

None.

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