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CASE REPORT

Salivary Duct Carcinoma Arising in a Warthin Tumor of the Parotid Gland: A Rare Case Report with Review of Literature and PD-L1 Expression

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Abstract

Warthin's tumor is the second most common neoplasm of the parotid gland and consists of 2 components, including lymphoid stroma and glandular epithelium. Malignant transformation in this tumor is mostly seen in the lymphoid component; however, the carcinomatous transformation of the epithelial component is extremely rare. Cases of latter reported in the literature include squamous cell carcinoma, adenocarcinoma, mucoepidermoid carcinoma, oncocytic carcinoma, Merkel cell carcinoma, and undifferentiated carcinoma. We describe an extremely rare case of salivary duct carcinoma arising in a Warthin tumor in a 64-year-old male. Patient presented with an enlarging left parotid mass, biopsy of which showed salivary duct carcinoma. He subsequently underwent left parotidectomy along with left level II–IV lymph node dissection. Histology revealed both in situ as well as invasive salivary duct carcinoma arising from Warthin tumor. Immunohistochemistry showed tumor cells positive for CK7, AR, and GATA3, while p63 highlighted the myoepithelial cell layer in the in situ component. Her2 was 2+ by immunohistochemistry. In addition, PD-L1 IHC revealed positive expression with a combined positive score of 20%.

Keywords Warthin tumor · Salivary duct carcinoma · Androgen receptor · PD-L1

Introduction

Warthin tumor (WT) is a benign salivary gland tumor with a predilection for the parotid gland. It is the second most common salivary gland tumor, representing approximately 5–15% of salivary gland neoplasms. They typically present in the sixth or seventh decade of life, have a slight predilection for males, and are associated with tobacco smoking [1]. The pathogenesis is currently thought to be from entrapped salivary duct epithelium in intraparotid lymphoid tissue [2]. Malignant transformation is more common in the lymphoid component but has been described in the epithelial component as well (0.1–0.3%) [3, 4], with mucoepidermoid carcinoma as the most frequently reported malignant tumor [2–12].

Salivary duct carcinoma (SDC), in contrast, is a highly aggressive malignancy, often resembling ductal carcinoma of the breast, with high-grade cytology, comedonecrosis, and cribriform architecture [13]. SDC represents approximately 5–10% of salivary gland malignancies, commonly affects middle-aged men with a mean age of 67.4 years, and largely arises in the parotid gland either de novo or from ex pleomorphic adenoma [13, 14]. Diagnosis of SDC is assisted by a strong and diffuse staining for androgen receptor (AR), GATA3, and Her2 (seen in 16–83% of cases) [15].

SDC arising in a Warthin tumor is extremely rare with only one case reported in English literature [16]. Herein, we describe a case of salivary duct carcinoma arising in a WT and concurrent literature review.

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Case Presentation

Clinical History

A 64-year-old male with comorbidities including hypertension, diabetes, and tobacco use presented for otolaryngology consultation for evaluation of a left parotid mass present over one year.

Imaging

Magnetic resonance imaging shows a lobular, enhancing infiltrative mass in the left parotid gland (4 cm × 2.4 cm) centered in the superficial and deep parotid and extending to parotid tail. Adjacent pathologic adenopathy (3 cm × 2.1 cm) in the external jugular chain is also noted (Fig. 1).

Needle Core Biopsy

A needle core biopsy of the left parotid was performed at an outside hospital and reported as salivary duct carcinoma, high grade, with no intact parotid salivary gland identified. Tumor cells were diffusely positive for CK7, mammaglobin, GCDFP, and androgen receptor (AR).

Surgery

Patient was referred to department of Otolaryngology, University of New Mexico where he underwent a left superficial parotidectomy with facial nerve preservation and left neck dissection of levels IIA, IIB, III, and IV. Additional deep parotid tissue with concerning appearance (below the plane of the marginal mandibular nerve) was excised.

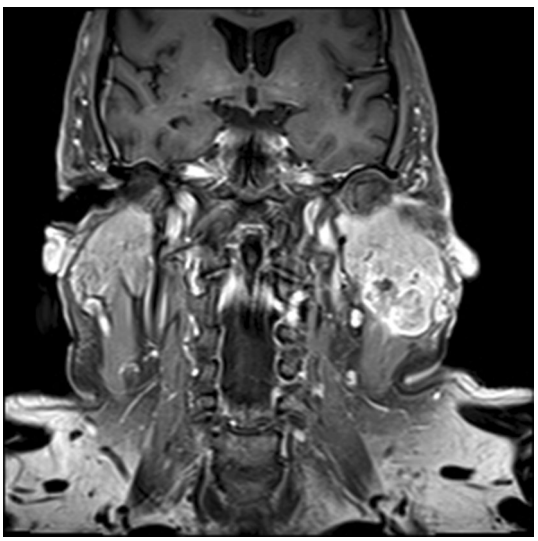

Fig. 1 MRI shows a lobular, enhancing infiltrative mass in the left parotid gland centered in the superficial and deep parotid and extending to parotid tail. Adjoining pathologic adenopathy is seen in the external jugular chain

Pathology

Grossly, the left parotidectomy showed three flesh-colored homogenous nodules, all measuring 2.5 cm in greatest dimension and containing small calcifications. The left neck dissection identified two lymph nodes grossly positive for tumor.

Histologic sections revealed diffuse infiltration of the gland parenchyma by high-grade salivary duct carcinoma, both invasive and in situ components, with classical oncocytic cytomorphology. The background parenchyma showed features of chronic sialadenitis and areas of classic Warthin tumor, including foci of in situ salivary duct carcinoma arising within Warthin's tumor with clear transition and intermingling of the tumors (Figs. 2A, B and F and 3E and F). Figures 4 and 5 show both WT and SDC components with 6B showing transformation of the bland eosinophilic WT epithelium to atypical hyperchromatic SDC cells. Figures 4 and 5 are snapshots from the Whole slide image of the tumor using the ImageScope browser software (Leica Biosystems, Inc.).

Lymphovascular invasion and cancerization of the native ducts were present (Fig. 3C–D). No perineural invasion was identified; however, extra parenchymal extension was present. The in situ component showed multilayered neoplastic epithelium with roman bridging and comedonecrosis akin to ductal carcinoma in situ seen in breast carcinoma. The individual cells in the in situ component showed moderate atypia with abundant oncocytic cytoplasm, vesicular nuclei, and prominent nucleoli. Immunohistochemistry showed tumor cells positive for CK7 (Dako, Santa Clara, CA), GATA3 (Ventana Roche, Oro Valley, AZ), and AR (Cell Marque, Rocklin, CA), with p63 and p40 (both from BioCare Medical, Pacheco, CA) highlighting the intact myoepithelial cells of the in situ component (Fig. 6A (inset). P63 also highlighted the basal layer in the WT component (Fig. 2G).

Her2neu IHC (Ventana Roche Oro Valley, AZ) showed positive expression of 2+ with subsequent FISH study negative for Her2 amplification. (Fig. 4E). In addition, PD-L1 IHC showed positive expression in tumor cells and intervening inflammatory cells, with a combined positive score (CPS) of 20. IHC for Cam5.2 (BD, San Jose, CA) showed positive expression in the extrafollicular reticulum cells (ERCs, Fig. 3B), confirming the origin of the tumor within a lymph node from Warthin tumor. In addition, Ki-67 (Ventana Medical Systems, Oro Valley, AZ) was performed and showed higher expression (~ 20, 50, and 5% in Intraductal component, invasive SDC, and WT respectively, Fig. 2 C–D).

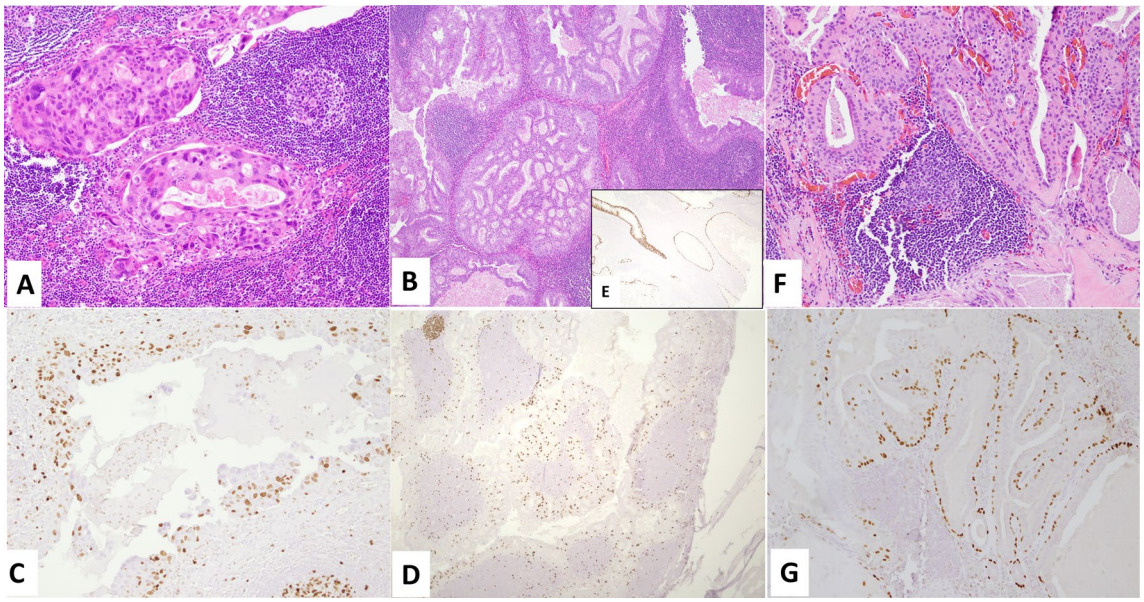

Fig. 2 **A** Nests of invasive salivary duct carcinoma; **B** In situ salivary duct carcinoma; **C** and **D** Images showing Ki-67 proliferation index in Invasive SDC and in situ component. **E** (Inset): p40 highlights the myoepithelial cell layer in the in situ component within the lymph node. **F** Residual Warthin tumor, **G** p63 is positive in the basal layer in Warthin tumor. Magnification for **A**, **C**, **F**, and **G** is 10x, while **B**, **D** and **E** is 4x. **A**, **B** and **F** are H&E stains

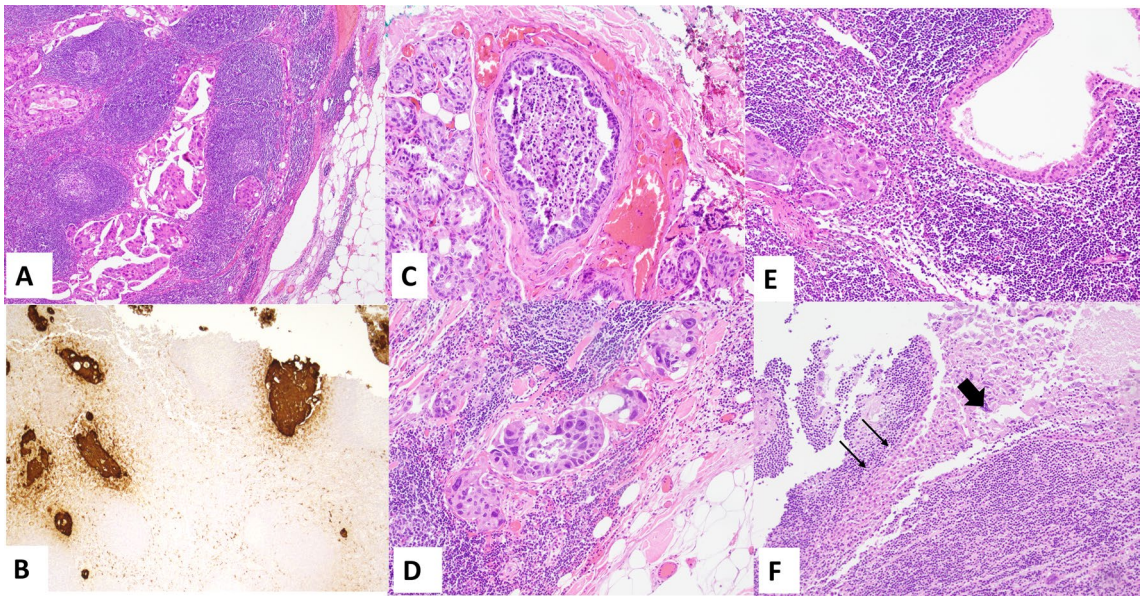

Fig. 3 **A** Nests of SDC within the lymph node, **B** Cam5.2 highlights the extrafollicular reticulum cells in the lymph node. **C** Cancerization of the duct; **D** Vascular invasion. **E** Both WT and SDC components side by side. **F** Transition from benign eosinophilic WT lining to atypical pleomorphic in situ SDC. Magnification for **A** and **B** is 4x. **C–F** is 10x. **A**, **C–F** are H & E

A total of 38 lymph nodes were examined from the neck dissection as well as from the intraparotid and peri parotid tissue, 14 of which were positive for metastatic carcinoma. No evidence of direct extension of tumor beyond the capsule was identified, however; soft tissue deposits adjoining lymph node capsule were seen. The tumor was staged as pT3 pN3b.

Post-surgery, the patient switched care to an outside institution for post-surgical management, the follow-up for which is unavailable.

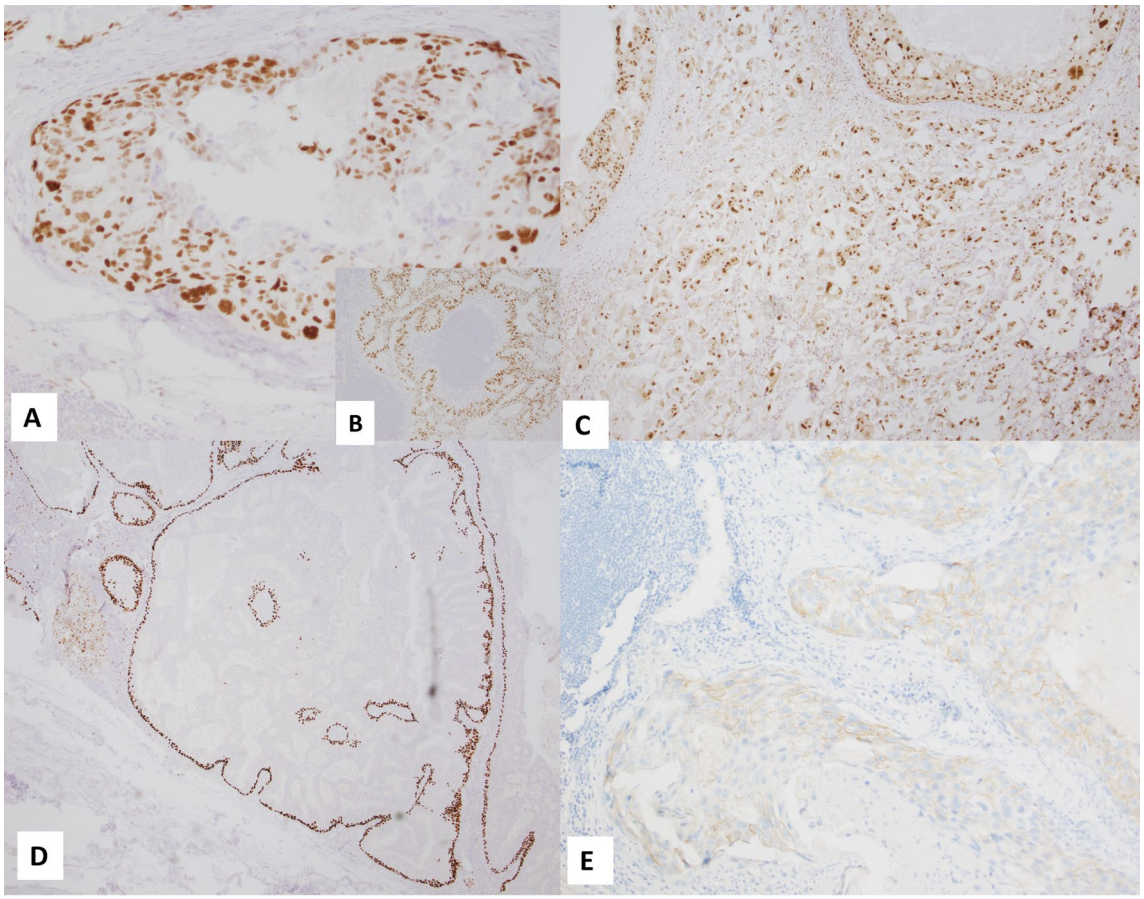

Fig. 4 Immunohistochemistry reveals **A** Positive Androgen receptor in invasive and in situ carcinoma (Inset, **B**); **C** GATA3 expression; **D** p63 is intact in the in situ component; **E** Her2 is 2+ by IHC. Magnification for **A**, **B,** and **E** is 10x; **C**-**D** is 4x, H & E

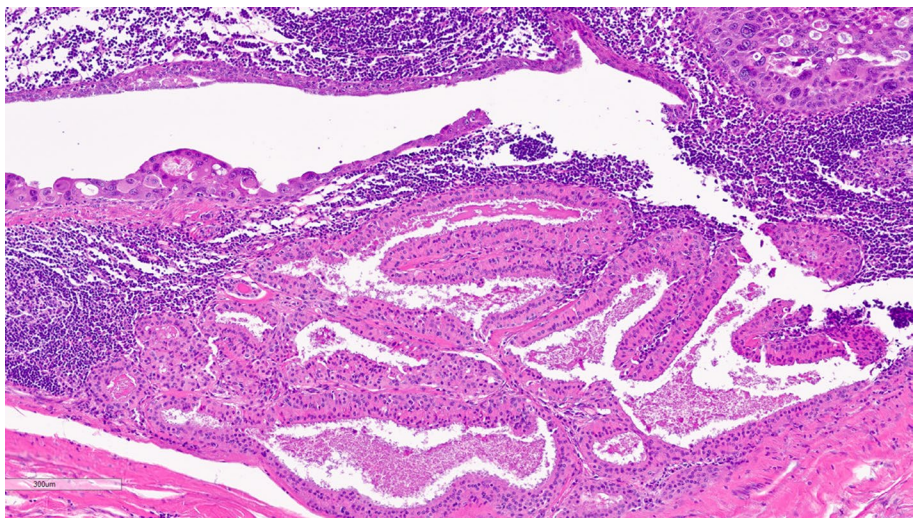

Fig. 5 Low-power image of in situ SDC arising from Warthin tumor in a lymph node (5x, H & E, snapshot from whole slide image)

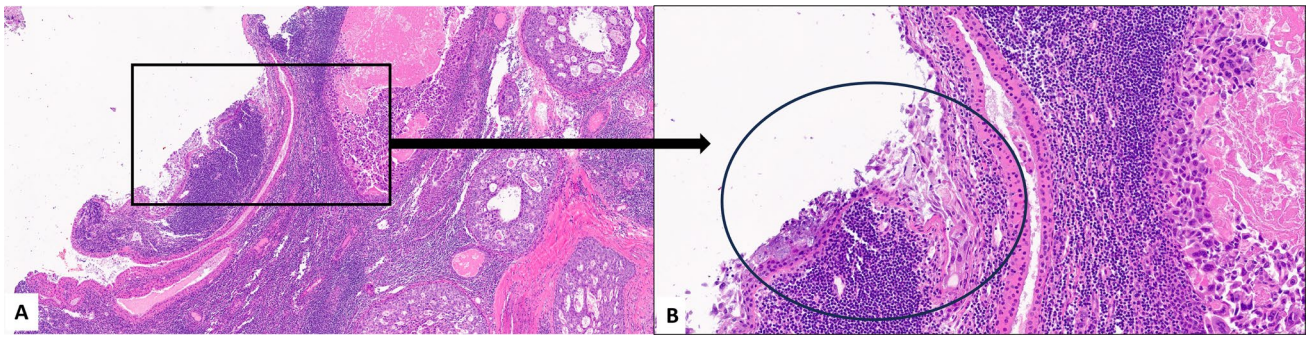

Fig. 6 **A** Low-power view of residual WT (bilayered epithelium) with adjoining in situ SDC; **B** Zoomed in image of the focus highlighted by a box in figure **A** showing transformation of benign epithelium into atypical, hyperchromatic malignant cells. Magnification for **A** is 5x, and **B** is 10x, snapshots from whole slide image

Discussion

Warthin tumor is a benign salivary gland tumor, accounting for up to 15% of salivary gland tumors [1]. It has been referenced as other names in the literature, including adenolymphoma and papillary cystadenoma lymphomatosum. Malignant transformation of the lymphoid component has been described more commonly than malignant transformation of the epithelial component with reported rates for the latter to be approximately 0.1–0.3% [3, 4].

The first case of adenocarcinoma arising in a WT was described by Ruebner and Bramhall in 1960 [17], following which, 52 additional cases have been reported in the English literature (Table 1). The reported age range is from 9 to 80 years, with only 2 reports of pediatric patients (age < 18 years) [18, 19] and, M:F ratio is > 2:1. The most frequently reported malignant counterpart was mucoepidermoid carcinoma (MEC), followed by squamous cell carcinoma, adenocarcinoma, oncocytic carcinoma, and poorly differentiated and undifferentiated carcinoma in that order of frequency. The cases previously described as MEC arising in WT is currently debatable since the discovery of the new variant WT-like MEC [20, 21]. We add an additional case of SDC arising in a Warthin tumor.

Our literature review identified only one prior case report of a salivary duct carcinoma arising in a Warthin tumor [16]. In contrast to the benign indolent nature of WT, salivary duct carcinoma is a highly aggressive tumor, first described in 1968, relating the histologic appearance to breast carcinoma, and was originally considered rare [50]. However, it is now recognized as not infrequent, accounting for up to 10% of salivary gland malignancies, and demonstrates high rates of local recurrence and distant metastases. Clinically, SDC presents as a rapidly growing tumor and radiographically shows features of malignant tumor, including ill-defined borders, invasion, and necrosis [15].

SDC can have in situ and invasive components, with rare reports of purely in situ SDC. Intraductal components are identified by characteristic architecture, including cribriform, solid, papillary, and "Roman bridges," whereas an invasive component is associated with invasion into surrounding tissues in form of nest, cords, and/or single cells [51]. SDC demonstrates high-grade cytologic atypia, comedonecrosis, and abundant mitoses. Cells are highly pleomorphic and often have abundant eosinophilic/ oncocytic cytoplasm. Lymphovascular and perineural invasion is common. Androgen receptor is expressed in 70% of cases, whereas it is only expressed in approximately 10% of other salivary gland tumors, and up to 30% of cases have overamplification of Her2 [14, 15].

Prior to the routine use of special and immunohistochemical stains, electron microscopy was used in several case reports. By electron microscopy, the characteristic oncocytic cells of WT demonstrate abundant mitochondria, and multiple authors describe a gradual transition from the large oncocytic cells to a separate population of cells with fewer mitochondria and increased intermediate and tonofilaments with fewer organelles in a malignant transformation to squamous cell carcinoma, oncocytic carcinoma, and mucoepidermoid carcinoma [14, 26, 28, 29, 33]. By special stains, mucoepidermoid mucous cells were commonly confirmed by positive staining for PAS, mucicarmine, and/or Alcian blue [3–5, 8, 12, 29, 33]. Skalova et al. [35], Therkildsen et al. [33], and Bolat et al. [39], all describe a discontinuous basal lamina around the carcinomatous component by electron microscopy or staining for collagen type IV and laminin. By immunohistochemistry, cytokeratins and EMA were commonly described as positive in benign and malignant epithelium, and Ki-67 expression was routinely seen more in the carcinomatous component than the benign WT component (3–4, 11, 30–31]. Molecular testing was not performed in these cases based on our literature review.

The single previously reported case of SDC arising with WT was reported by Kim et al. [16] in which they describe a component of SDC, confirmed by positive staining for GCDFP and AR, as well as membranous staining for Her2.

Table 1 Clinical and pathologic findings of the SDC-ex-WT cases reported in the literature (chronologic order)

Authors	Year	Age/sex	Histopathology	Patient outcomes	Molecular data (if available)
Ruebner and Bramhall [17]	1960	67 M	Adenocarcinoma	Deceased 10 years later	N/A
Little and Rickles [22]	1965	78 M	Adenocarcinoma	Deceased 1 year later of unrelated disease	N/A
De la Pava et al. [23]	1965	72 M	Squamous cell carcinoma	1 year NED	N/A
Assor [24]	1974	58 M	Squamous cell carcinoma	N/A	N/A
Gadient and Kalfayan [9]	1975	60 M	Mucoepidermoid carcinoma	6 years NED	N/A
Kessler et al. [25]	1977	63 M	Adenocarcinoma	Deceased 4 years later with distant metastases	N/A
Caldwell et al. [26]	1979	33 M	Undifferentiated carcinoma	2 years NED	N/A
McClatchey et al. [27]	1982	59 M	Squamous cell carcinoma	1 year NED	N/A
Damjanov et al. [28]	1983	72 M	Squamous cell carcinoma	N/A	N/A
Nakashima et al. [29]	1983	73 M	Oncocytic adenocarcinoma/ Acinic cell carcinoma	13 months NED	N/A
Brown and Aparicio [30]	1984	68 F	Oncocytic adenocarcinoma	2 years NED	N/A
Bengoechea et al. [31]	1989	67 M	Oncocytic adenocarcinoma	Deceased 5 months later of disease	N/A
Onder et al. [32]	1990	77 M	Adenocarcinoma	Lung metastases 11 months after treatment	N/A
Therkildsen et al. [33]	1992	69 M	Oncocytic adenocarcinoma	N/A	N/A
Podlešák et al. [34]	1992	79 M	Undifferentiated carcinoma	3 years NED	N/A
Skalova et al. [35]	1994	80 F	Epidermoid/Squamous cell carcinoma	Deceased 5 years later of unrelated disease	N/A
Saku et al. [7]	1997		Mucoepidermoid carcinoma	66 F	N/A
Siefert [5]	1997	73 M	Mucoepidermoid carcinoma	NED (time not specified)	N/A
Nagao et al. [4]	1998	58 M	Mucoepidermoid carcinoma	2 years 6 months NED	N/A
		54 F	Mucoepidermoid carcinoma	2 years 10 months NED	N/A
Gunduz et al. [36]	1999	71 F	Squamous cell carcinoma	2 years NED	N/A
Williamson et al. [6]	2000	45 F	Mucoepidermoid carcinoma	N/A	N/A
		40 M	Mucoepidermoid carcinoma	4 years 4 months NED	N/A
		39 M	Mucoepidermoid carcinoma	N/A	N/A
		60 M	Mucoepidermoid carcinoma	2 years 6 months NED	N/A
		70 F	Mucoepidermoid carcinoma	8 months NED	N/A
Yamada et al. [37]	2002	64 M	Mucoepidermoid carcinoma	1 year 7 months NED	N/A
Ferrero et al. [38]	2003	73 M	Poorly differentiated adenocarcinoma	1 year 8 months NED	N/A
Bolat et al. [39]	2004	48 F	Epidermoid/Squamous cell carcinoma	6 months NED	N/A
Foschini et al. [40]	2004	72 F	Oncocytic adenocarcinoma	Skin metastases 10 months after treatment	N/A
Perrotti et al. [41]	2005	49U	Adenocarcinoma	7 years NED	N/A
Mardi and Sharma [8]	2007	35 F	Mucoepidermoid carcinoma	N/A	N/A
Moore et al. [42]	2007	50 M	Poorly differentiated adenocarcinoma	2 years NED	N/A
Sharma et al. [19]	2008	16 F	Squamous cell carcinoma	1 year NED	N/A
Bell and Luna [43]	2009	44 F	Adenocarcinoma	1 year NED	N/A
		60 F	Adenocarcinoma	3 years NED	N/A
Deodhar et al. [44]	2011	75 M	Adenocarcinoma	N/A	N/A
Kim et al. [16]	2011	79 M	Salivary duct carcinoma	N/A	Focal amplification 12q14-q21.2 (including MDM2 region), Her2 ISH focal amplification, loss of heterozygosity at p16.

Table 1 (continued)

Authors	Year	Age/sex	Histopathology	Patient outcomes	Molecular data (if available)
Sayar et al. [45]	2012	63 M	Adenocarcinoma	1 year NED	N/A
Mohaptra and Satyanarayana [2]	2012	55 F	Mucoepidermoid carcinoma	N/A	N/A
Yaranal and Umashankar [46]	2013	65 M	Squamous cell carcinoma	N/A	N/A
Allevi and Biglioli [47]	2014	60 M	Squamous cell carcinoma	1 year NED	N/A
Smolka et al. [11]	2015	61 M	Mucoepidermoid carcinoma	N/A	N/A
Yu et al. [3]	2016	43 F	Mucoepidermoid carcinoma	2 years 1 month NED	N/A
	2016	40 M	Mucoepidermoid carcinoma	2 years NED	N/A
	2016	63 M	Mucoepidermoid carcinoma	5 years 3 months NED	N/A
	2016	26 F	Mucoepidermoid carcinoma	5 years 9 months NED	N/A
	2016	56 M	Mucoepidermoid carcinoma	2 years 1 month NED	N/A
Hakeem et al. [10]	2016	73 F	Mucoepidermoid carcinoma	Deceased 3 years later of unrelated disease	N/A
Nguyen et al. [48]	2018	63 M	Squamous cell carcinoma/ Adenocarcinoma	6 months NED	N/A
Citak et al. [18]	2018	9 F	Mucoepidermoid carcinoma	10 months NED	N/A
Kim and Kim [49]	2019	68 M	Squamous cell carcinoma	N/A	N/A
Jamshidi et al. [12]	2021	36 F	Mucoepidermoid carcinoma	5 years NED	N/A
Current case	2021	64 M	Salivary duct carcinoma	Patient received radiation therapy at an outside facility, records unavailable	NGS did not identify any fusion transcripts

NED no evidence of disease, *IHC* immunohistochemistry, *SS* special stains, *EM* electron microscopy, *WT* Warthin tumor, *MEC* mucoepidermoid carcinoma, *SDC* salivary duct carcinoma, *NGS* Next-generation sequencing

Molecular studies were performed in this case and demonstrated Her2 amplification, loss of heterozygosity at p16, and focal amplification at the 12q14-q21.2 locus, which includes the region of MDM2. This case also reported 11 lymph nodes positive for metastatic disease at the time of resection [16]. Similarly in the current case, the SDC component was positive for AR, GCDFP, and mammaglobin, and Her2 had membranous staining reported as 2+. FISH studies were negative for Her2 amplification. Fourteen lymph nodes were positive for metastatic disease at the time of resection. Both cases of SDC arising in WT demonstrate the high aggression correlated with SDC. Next-generation sequencing was performed in the current case (Neo Genomics Salivary gland fusion panel included MAML1/2, ETV6, ARID1A, ATF1, HMGA2, NTRK1/3, PLAG1, PRKD2, RET, USP6 among others); however, the analysis did not identify any molecular aberration.

SDC most commonly occurs as the malignant component in carcinoma ex pleomorphic adenoma or de novo [14]. Extremely rarely, as in this case, it can arise as the malignant component of a transformed Warthin tumor. Given the rarity of epithelial neoplasia in WT, it is crucial to first exclude the more common other possibilities, including a co-existing but separate synchronous tumor and metastasis from a separate distant tumor to the lymphoid stroma [2, 3]. Multiple sections in our case showed a transition of the benign WT epithelial cell into markedly atypical cells of in situ component (Fig. 2D and 3A).

The differential diagnosis for SDC itself includes both primary salivary gland tumors and metastatic carcinoma. High-grade mucoepidermoid carcinoma or high-grade transformation of any primary salivary gland tumors can be a diagnostic challenge. In these instances, it is prudent to carefully look for lower-grade areas and areas of classic histology for these primary tumors. Additionally, metastatic squamous cell carcinoma must be excluded; immunohistochemistry for p63/p40, and CK5/6 will be positive in SCC while AR and GATA3 should help in identifying SDC. Metastatic carcinoma from other sites such as breast or prostate can also look very similar, considering SDC was identified based on its similar morphology to high-grade breast carcinoma. Immunohistochemistry for sites of origin, as well as ER and PR, is helpful in these cases [43, 52].

When considering a malignant transformation of WT, it is important to rule out possibility of synchronous tumors arising in the salivary gland. While WT and mucoepidermoid carcinoma are the most common co-existing tumors in salivary glands, Bulut et al. [53] recently reported co-existing SDC and WT, while Fornelli et al. [54] reported two cases of Merkel cell carcinoma arising in close association with WT. Skalova et al. [29, 1994] and later Siefert [5, 1997] published the criteria for diagnosing malignant transformation in WTs:

1. The presence of a pre-existing WT.
2. Presence of transition zones from benign WT oncocytic epithelium to malignant epithelium.
3. Infiltrative growth into surrounding lymphoid stroma.
4. Exclusion of metastases of distant tumor to the lymphoid stroma.

These criteria accurately exclude the possibility of synchronous tumors by requiring the identification of transition zones between benign and malignant epithelium. Additionally, the fourth criterion is important to recognize and communicate with clinicians, requiring thorough assessment of clinical history and radiography. Immunohistochemistry and special staining for markers such as PAS and mucicarmine, AR, collagen IV/laminin, p63, and Ki-67 may be of diagnostic use when reviewing histopathology. Cam5.2 can help differentiate between tumor associated lymphoid proliferation (TALP) vs. true lymph node stroma in addition to the presence of a discrete capsule and sinuses in the latter [55]. In addition to supportive morphology for a LN, Cam5.2 highlighted the ERCs further confirming our impression.

Complete surgical excision with adequate margins is generally considered curative for WT [1]. However, due to the high rates of local recurrence and distant metastases for SDC, management varies. Initial treatment begins with complete surgical resection, often followed by postoperative radiation therapy. Depending on tumor stage, patients may also receive a neck dissection. For metastatic or recurrent unresectable disease, patients may undergo cytotoxic chemotherapy. Androgen deprivation therapy and Her2-targeted therapy have also shown response in recurrent disease [13, 15]. As many as 65% of patients with SDC succumb to the disease [14].

Anti-PD-1 (PD-1 is a transmembrane glycoprotein when activated, can inhibit cytotoxic T-Cell immune response, leading to immune tolerance by tumor cells) therapy in the form of Pembrolizumab has been approved by US Food and Drug administration for metastatic non-small cell lung carcinoma [56]. Its efficacy in advanced salivary gland cancers was analyzed by Cohen et al. [57] who found the drug's promising antitumor activity and a manageable safety profile. Immunohistochemistry for PD-L1 showed positive expression with a CPS score of 20% in the current case, making patient amenable to receive immunotherapy. However, we are not aware of the use of immunotherapy for this patient post-surgery as patient changed his care to an outside hospital.

The vast majority of cases (in this review) were treated with varying combinations of surgery, chemotherapy, and radiotherapy, with no evidence of disease post treatment. Four cases were reported to have lymph node metastases at the time of resection [10, 16, 32, 48]. One case was reported to have intracranial metastases at the time of presentation of oncocytic carcinoma and subsequently died of the disease 5 months later [31]. Two cases reported distant metastases, including skin metastases of oncocytic carcinoma at 10 months and lung metastases of adenocarcinoma at 11 months [35, 48].

Although pathogenesis of malignant transformation of WT is unknown, it is of special interest that WT had undergone radiation therapy before malignant transformation in multiple previously reported cases [7, 17, 22, 23]. Saku et al. reported a case of MEC in a pre-existing WT related to radiation exposure at Hiroshima [7]. We are not aware of any radiation exposure in the current patient.

Conclusion

Salivary gland neoplasms often pose diagnostic challenges due to their significant morphologic overlap. The current case represents an extremely rare case of SDC-ex-WT, only the second report of such a diagnosis (to the best of our knowledge).

While carcinoma ex pleomorphic adenoma is well understood by now, malignant transformation of the epithelial component of WT is exceedingly rare and is reported mostly in association with squamous cell carcinoma, mucoepidermoid carcinoma, and adenocarcinoma, among others. Definitive identification of carcinoma ex WT relies on adhering to the diagnostic criteria for the same and exclusion of metastases.

The identification of SDC as the carcinomatous component of carcinoma ex WT is important as the prognosis of SDC is extremely poor, and management requires multimodality therapy for recurrent or metastatic disease. This case emphasizes the importance of recognizing the rare phenomenon of malignant transformation in Warthin tumors, and the importance of diagnosing SDC arising in WT for management and prognostic purposes. In addition, expression of PD-L1 opens a new area for future studies to explore possibility of immunotherapy in these aggressive tumors.

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Declarations

Conflict of interest The authors declare no competing interests.

Ethical Approval Not applicable.

Consent to Participants Not applicable.

Consent for Publication Not applicable.

Research Involving Humans and Animals No patient's personal data/identifiers are disclosed; hence, no consent was taken.

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