Polymorphous Low Grade Adenocarcinoma has a Consistent p63+/p40– Immunophenotype that Helps Distinguish it from Adenoid Cystic Carcinoma and Cellular Pleomorphic Adenoma

Lisa Rooper · Rajni Sharma · Justin A. Bishop

Received: 30 April 2014 / Accepted: 21 June 2014 / Published online: 27 June 2014
© Springer Science+Business Media New York 2014

Abstract Polymorphous low grade adenocarcinoma (PLGA) is a tumor of minor salivary glands that exhibits considerable morphologic overlap with adenoid cystic carcinoma and cellular pleomorphic adenoma, especially in small biopsy specimens. Unlike these other tumor types, PLGAs do not harbor a myoepithelial component, yet their frequent positivity for p63 diminishes the usefulness of this particular myoepithelial marker as a discriminating immunostain. p40 is an antibody that recognizes Δ Np63, a p63 isoform that is more specific for true myoepithelial differentiation. As such, p40 immunostaining could help distinguish PLGAs from adenoid cystic carcinomas and pleomorphic adenomas. In this study, p63 and p40 immunohistochemistry was performed on paraffin embedded, formalin fixed tissue from 11 PLGAs, 101 adenoid cystic carcinomas, and 31 pleomorphic adenomas. All 11 PLGAs (100 %) were positive for p63 but completely negative for p40. Among adenoid cystic carcinomas, 91 of 101 (90 %) were positive for p63 and 90/101 (89 %) were positive for p40. The single discordant p63+/p40– adenoid cystic carcinoma exhibited solid architecture and high grade features

not typically seen in PLGA. Among pleomorphic adenomas, 21/31 (68 %) were positive for p63 and 13/31 (42 %) were positive for p40. For the pleomorphic adenomas, the discordant p63+/p40– staining pattern was seen only in the overtly mesenchymal chondromyxoid stroma. The cellular epithelial component of the pleomorphic adenomas demonstrated concordant p63+/p40+ or p63–/p40– immunophenotypes. PLGA consistently exhibits a p63+/p40– immunophenotype that can help distinguish it from adenoid cystic carcinoma and cellular pleomorphic adenoma, tumors that characteristically demonstrate concordant p63 and p40 immunostaining patterns. A p63/p40 immunohistochemical panel can provide a valuable tool for making the distinction between these morphologically similar but clinically divergent entities.

Keywords Polymorphous low grade adenocarcinoma · Adenoid cystic carcinoma · Pleomorphic adenoma · p63 · p40

Background

Polymorphous low grade adenocarcinoma (PLGA) is a tumor that almost exclusively affects minor salivary glands and comprises the third most common malignant salivary gland tumor in the oral cavity [1–7]. Although PLGAs have many distinctive features, including optically clear chromatin and a targetoid pattern of perineural invasion, the architectural heterogeneity that their name reflects can create a diagnostic dilemma for pathologists. PLGAs can demonstrate multiple patterns of growth including solid, trabecular, glandular, cribriform, fascicular, cord-like, and papillary configurations [1–4, 8]. As such, they exhibit considerable morphologic overlap with other salivary neoplasms, especially adenoid cystic carcinoma and cellular pleomorphic adenomas [1, 2].

The abstract of this article was presented as a poster at the 2014 Annual Meeting of the United States and Canadian Academy of Pathology, San Diego, CA, USA.

L. Rooper · R. Sharma · J. A. Bishop
Departments of Pathology, The Johns Hopkins Medical Institutions, Baltimore, MD, USA

J. A. Bishop
Departments of Otolaryngology/Head and Neck Surgery, The Johns Hopkins Medical Institutions, Baltimore, MD, USA

J. A. Bishop (✉)
The Johns Hopkins University School of Medicine, 401 N. Broadway, Weinberg 2249, Baltimore, MD 21231, USA
e-mail: jbisho16@jhmi.edu; jbishop@jhmi.edu

Because of the considerable difference in prognosis, treatment, and follow up for these three neoplasms, there is a clinical imperative to accurately distinguish PLGAs from these two mimickers. However, while many immunohistochemical stains (e.g., c-kit, Ki-67, glial fibrillary acidic protein, CD43, S100, bcl-2, etc.) have been used to aid in this differential diagnosis, none of them distinguishes these tumors in a consistently reliable manner [9–20].

A potential basis for differentiating these three lesions is the fact that pleomorphic adenomas and adenoid cystic carcinomas harbor a prominent myoepithelial component, while PLGAs show no compelling immunohistochemical or ultrastructural evidence of true myoepithelial differentiation [21–23]. p63 is an immunohistochemical marker that is normally expressed in the basal layer of stratified epithelium, myoepithelial cells, and neoplasms that derive from these epithelia [24]. However, p63 has proven surprisingly unhelpful in distinguishing between PLGA, adenoid cystic carcinoma, and pleomorphic adenoma, as it often shows strong and diffuse positivity in PLGA despite its lack of myoepithelial differentiation [23, 25, 26]. Similar aberrant p63 immunolabeling has been seen in lung adenocarcinomas, soft tissue neoplasms, and lymphomas [27–30]. Recently, the antibody to p40, an isotype of p63, has emerged as a more specific marker of basal and myoepithelial cell differentiation [29–32]. Consequently, it is possible that p40 might also prove more useful than p63 for differentiating PLGA from adenoid cystic carcinoma and pleomorphic adenoma.

Materials and Methods

Formalin fixed and paraffin embedded tissue blocks from 143 salivary gland tumors were retrieved from the Surgical Pathology archives of The Johns Hopkins Hospital. These cases included 11 PLGAs, 101 adenoid cystic carcinomas, and 31 pleomorphic adenomas. Eight of the PLGAs were stained on whole sections, while the remaining 135 tumors were evaluated using previously constructed tissue microarrays. The tissue microarrays included three or four 1 mm punches from different areas of the tumors to address the issue of tumor heterogeneity.

Immunohistochemistry for p63 (4A4; BioCare Medical, Concord CA) and p40 (BC28, BioCare Medical, Concord CA) was performed on five-micron tissue sections. Antigen retrieval was completed using high pH buffer, followed by primary antibody incubation for 32 min. The samples were then stained using a Ventana BenchMark ULTRA automated stainer and an ultraView detection system according to manufacturer's instructions (Ventana Medical Systems Inc. Tucson, AZ). Any nuclear positivity was regarded as positive.

Results

The results are summarized in Table 1. Consistent with previous reports, all 11 PLGAs (100 %) demonstrated nuclear positivity for p63, usually in a diffuse manner. All 11 of these PLGAs also demonstrated a complete lack of staining for p40 (0 %). Accordingly, 11 of 11 (100 %) PLGAs in this study can be described as having a discordant p63+/p40– immunophenotype (Fig. 1a–c).

Among adenoid cystic carcinomas, 91 of 101 tumors (90 %) showed nuclear positivity for p63. In addition, 90 of 101 (89 %) adenoid cystic carcinomas were also positive for p40 (Fig. 1d–f). Both the p63 and p40 staining in these tumors often demonstrated a peripheral (abluminal) labeling pattern, with staining in myoepithelial cells but not ductal cells. There was only 1 of 101 (1 %) adenoid cystic carcinomas that demonstrated rare p63+ tumor cells in the absence of p40+ tumor cells (Fig. 2a–c). This tumor had solid architecture and high grade histologic features including numerous mitotic figures and necrosis. The adenoid cystic carcinomas that were negative for both p63 and p40 were also solid and high grade.

Among pleomorphic adenomas, 21 of 31 tumors (68 %) demonstrated positivity for p63 while 13 of 31 (42 %) pleomorphic adenomas also stained positive for p40 (Fig. 1g–i). As in adenoid cystic carcinomas, the p63 and p40 staining often demonstrated a peripheral (myoepithelial cell) pattern. There were 8 of 31 (26 %) pleomorphic adenomas that demonstrated a p63+/p40– phenotype. In these discordant tumors, the nuclear p63 staining was seen in cells in well-developed chondromyxoid stroma (Fig. 2d–f). All of the cellular ductal components of the pleomorphic adenomas demonstrated concordant p63+/p40+ or p63–/p40– immunophenotypes.

Overall, among PLGAs, adenoid cystic carcinomas, and pleomorphic adenomas, a p40 negative immunophenotype was 100 % sensitive and 78 % specific for PLGA in itself. When both p63 and p40 staining patterns were considered in these same tumors, a discordant p63+/p40– immunophenotype was 100 % sensitive and 93 % specific for PLGA. If defining only cellular ductal epithelium staining as positive, the p63+/p40– immunophenotype was 100 % sensitive and 99 % specific for PLGA within this differential diagnosis (see Table 2).

Discussion

While polymorphous low grade adenocarcinoma has distinctive cytological features and a characteristic appearance of perineural invasion, its heterogeneous architecture can make for a difficult differential diagnosis with adenoid cystic carcinoma and cellular pleomorphic adenoma [1, 2].

Table 1 p63/p40 immunophenotypes in polymorphous low-grade adenocarcinoma, adenoid cystic carcinoma, and pleomorphic adenoma

	p63+/p40+	p63+/p40–	p63–/p40–
Polymorphous low-grade adenocarcinoma	0/11 (0 %)	11/11 (100 %)	0/11 (0 %)
Adenoid cystic carcinoma	90/101 (89 %)	1/101 (1 %)	10/101 (10 %)
Pleomorphic adenoma	13/31 (42 %)	8/31 (26 %)	10/31 (32 %)

Fig. 1 All polymorphous low grade adenocarcinomas (H&E, **a**) showed diffuse, strong, positivity for p63 (**b**) but complete negativity for p40 (**c**). In contrast, most of the adenoid cystic carcinomas

(H&E, **d**) and pleomorphic adenomas (H&E, **g**) demonstrated positivity for both p63 (**e**, **h**) and p40 (**f**, **i**) in a peripheral (myoepithelial cell) pattern

This problem is particularly pronounced on small biopsy specimens, where specific features of all three lesions may be absent or obscured. Indeed, recent consult series have reported that correct initial diagnosis of PLGA is made in as few as 22 to 43 % of cases [33, 34]. Furthermore, correctly differentiating these tumors at biopsy can have implications for surgical management. PLGA requires wider resection than pleomorphic adenoma, whereas adenoid cystic carcinoma can sometimes warrant elective neck dissection, a procedure which is not indicated in PLGA [35].

Because of the difficulty and importance of distinguishing PLGA from adenoid cystic carcinoma and pleomorphic adenoma, many previous studies have investigated ways to definitively separate these lesions. One useful point

of differentiation reported by Skalova et al. [36] and Vargas et al. [37] is the fact that adenoid cystic carcinomas have a significantly higher Ki-67 index than PLGAs, although other investigators have found exceptions to this trend [38]. In another promising finding, Penner et al. [15] and Epivatianos et al. [20] noted diffuse c-kit positivity in adenoid cystic carcinomas and negativity in PLGAs, but other groups found no difference in c-kit expression between these tumors [14]. Likewise, Gnepp et al. [9] and Curran et al. [12, 19] have noted glial fibrillary acidic protein to cross react with mesenchymal stroma in pleomorphic adenomas and not PLGAs, while other reports have described positivity in both neoplasms [8]. Additionally, Woo et al. [17] reported that CD43 is more strongly expressed in adenoid cystic carcinoma than

Fig. 2 The few adenoid cystic carcinomas and pleomorphic adenomas that demonstrated a discordant p63+/p40– immunophenotype did not show significant morphologic overlap with polymorphous low grade adenocarcinoma. One adenoid cystic carcinoma with

high-grade cytology and solid architecture (a) showed focal positivity for p63 (b) but complete negativity for p40 (c). In the overt chondromyxoid stroma of eight pleomorphic adenomas (d), diffuse positivity for p63 (e) and complete negativity for p40 (f) was seen

Table 2 Sensitivity and specificity of p63/p40 staining patterns for polymorphous low-grade adenocarcinoma

Staining pattern	Sensitivity (%)	Specificity (%)
p40–	100	78
Any p63+/p40–	100	93
Epithelial p63+/p40–	100	99

PLGA, a finding that has not yet been confirmed by other investigators. Unfortunately, other immunostains, including S100 and bcl-2, have not consistently helped differentiate PLGA from either adenoid cystic carcinoma or pleomorphic adenoma [13, 18, 39].

p63, an immunohistochemical stain that highlights basal and myoepithelial differentiation, has never routinely been used to distinguish between PLGA, adenoid cystic carcinoma, and pleomorphic adenoma because all three lesions are frequently positive for this marker [23, 25, 26]. However, while pleomorphic adenomas and adenoid cystic carcinomas have proven myoepithelial differentiation consistent with this staining pattern, no true myoepithelial component has been identified in PLGAs [21–23]. As such, the p63 staining in PLGAs appears likely to represent aberrant expression of the TAp63 isoform similar to that seen in lung adenocarcinomas, soft tissue tumors, and lymphomas, raising the possibility that a more myoepithelial-specific antibody may be able to distinguish these lesions. The antibody p40, specific for the ΔNp63 isotype of p63, has previously proven more specific for squamous

and myoepithelial differentiation in tumors of other anatomic sites [29–32].

Examining 143 salivary tumors, we confirmed previous reports of p63 positivity in PLGA. For the first time, we also established that PLGA demonstrates uniform p40 negativity, consistent with a lack of true myoepithelial differentiation in PLGA. However, p40 negativity was only 78 % specific for PLGA and does not provide an optimal discriminatory immunostain by itself. While most adenoid cystic carcinomas and pleomorphic adenomas were p40 positive, some stained negatively for both p63 and p40, a problem that could be compounded by limited sampling. In contrast, a combined p63/p40 panel better differentiated these lesions. Regardless of positivity or negativity, adenoid cystic carcinomas and pleomorphic adenomas generally demonstrated a concordant p63/p40 immunophenotype. Consequently, a discordant p63+/p40– immunophenotype provided 93 % specificity for identifying PLGA.

It is important to note that rare adenoid cystic carcinomas and pleomorphic adenomas can demonstrate a p63+/p40– immunophenotype. However, the tumors that showed this immunophenotypic overlap in the cases in this study were not those that presented pronounced morphologic concordance with PLGA. Indeed, the single adenoid cystic carcinoma that was p63+/p40– not only had solid architecture that is atypical for PLGAs, but also demonstrated high grade histologic features that should effectively rule out a PLGA diagnosis. Moreover, all eight p63+/p40– pleomorphic adenomas demonstrated the p63 staining only in cells in the overtly mesenchymal areas.

Indeed, while PLGA may exhibit some myxoid features, the well-developed chondroid and myxochondroid zones of pleomorphic adenoma are not seen [1, 2]. In neoplastic cellular ductal epithelium, the morphologically significant area of overlap between these three tumors, the p63+/p40– immunophenotype was 99 % specific for PLGA.

In summary, p40 immunostaining is a valuable new tool for distinguishing salivary gland tumors with true myoepithelial differentiation from those showing nonspecific p63 expression. When these immunostains are performed in tandem, a discordant p63+/p40– immunophenotype can reliably distinguish PLGA from both adenoid cystic carcinoma and pleomorphic adenoma, which generally show p63/p40 concordance. An unexpected p63+/p40– pattern can occur in high grade adenoid cystic carcinoma and the mesenchymal chondromyxoid component of pleomorphic adenomas. However, in most cases of morphologic overlap, a p63/p40 immunohistochemical panel can provide a useful adjunct for making the distinction between these clinically divergent entities.

Acknowledgments This study was funded in part by the National Institutes of Health/National Institute of Dental and Craniofacial Research (NIH/NIDCR) Head and Neck SPORE Grant P50 DE019032.

References

- Luna MA, Wenig BM. Polymorphous low-grade adenocarcinoma. In: Barnes L, Eveson JW, Reichart P, Sidransky D, editors. *Pathology and genetics of head and neck tumours*. Lyon: IARC Press; 2005. p. 223–4.
- Ellis GL, Auclair PL. Polymorphous low-grade adenocarcinoma. AFIP atlas of tumor pathology: tumors of the salivary glands. Washington, DC: ARP Press; 2008. p. 246–259.
- Frierson HF Jr, Mills SE, Garland TA. Terminal duct carcinoma of minor salivary glands. A nonpapillary subtype of polymorphous low-grade adenocarcinoma. *Am J Clin Pathol*. 1985;84:8–14.
- Aberle AM, Abrams AM, Bowe R, et al. Lobular (polymorphous low-grade) carcinoma of minor salivary glands. A clinicopathologic study of twenty cases. *Oral Surg Oral Med Oral Pathol*. 1985;60:387–95.
- Venkata V, Irulandy P. The frequency and distribution pattern of minor salivary gland tumors in a government dental teaching hospital, Chennai, India. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2011;111:e32–9.
- Kakarala K, Bhattacharyya N. Survival in oral cavity minor salivary gland carcinoma. *Otolaryngol Head Neck Surg*. 2010;143:122–6.
- Pires FR, Pringle GA, de Almeida OP, et al. Intra-oral minor salivary gland tumors: a clinicopathological study of 546 cases. *Oral Oncol*. 2006;43:463–70.
- Castle JT, Thompson LD, Frommelt RA, et al. Polymorphous low grade adenocarcinoma: a clinicopathologic study of 164 cases. *Cancer*. 1999;86:207–19.
- Gnepp DR, S el-Mofty. Polymorphous low-grade adenocarcinoma: glial fibrillary acidic protein staining in the differential diagnosis with cellular mixed tumors. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 1997;83:691–5.
- Loducca SV, Raitz R, Araujo NS, et al. Polymorphous low-grade adenocarcinoma and adenoid cystic carcinoma: distinct architectural composition revealed by collagen IV, laminin and their integrin ligands (alpha2beta1 and alpha3beta1). *Histopathology*. 2000;37:118–23.
- Araujo VC, Loducca SV, Sousa SO, et al. The cribriform features of adenoid cystic carcinoma and polymorphous low-grade adenocarcinoma: cytokeratin and integrin expression. *Ann Diagn Pathol*. 2001;5:330–4.
- Curran AE, White DK, Damm DD, et al. Polymorphous low-grade adenocarcinoma versus pleomorphic adenoma of minor salivary glands: resolution of a diagnostic dilemma by immunohistochemical analysis with glial fibrillary acidic protein. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2001;91:194–9.
- Darling MR, Schneider JW, Phillips VM. Polymorphous low-grade adenocarcinoma and adenoid cystic carcinoma: a review and comparison of immunohistochemical markers. *Oral Oncol*. 2002;38:641–5.
- Edwards PC, Bhuiya T, Kelsch RD. C-kit expression in the salivary gland neoplasms adenoid cystic carcinoma, polymorphous low-grade adenocarcinoma, and monomorphic adenoma. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2003;95:586–93.
- Penner CR, Folpe AL, Budnick SD. C-kit expression distinguishes salivary gland adenoid cystic carcinoma from polymorphous low-grade adenocarcinoma. *Mod Pathol*. 2002;15:687–91.
- Epivatianos A, Iordanides S, Zaraboukas T, et al. Adenoid cystic carcinoma and polymorphous low-grade adenocarcinoma of minor salivary glands: a comparative immunohistochemical study using the epithelial membrane and carcinoembryonic antibodies. *Oral Dis*. 2005;11:175–80.
- Woo VL, Bhuiya T, Kelsch R. Assessment of CD43 expression in adenoid cystic carcinomas, polymorphous low-grade adenocarcinomas, and monomorphic adenomas. *Oral Surg Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2006;102:495–500.
- Beltran D, Faquin WC, Gallagher G, et al. Selective immunohistochemical comparison of polymorphous low-grade adenocarcinoma and adenoid cystic carcinoma. *J Oral Maxillofac Surg*. 2006;64:415–23.
- Curran AE, Allen CM, Beck FM, et al. Distinctive pattern of glial fibrillary acidic protein immunoreactivity useful in distinguishing fragmented pleomorphic adenoma, canalicular adenoma and polymorphous low grade adenocarcinoma of minor salivary glands. *Head Neck Pathol*. 2007;1:27–32.
- Epivatianos A, Pouloupoulos A, Dimitrakopoulos I, et al. Application of alpha-smooth muscle actin and c-kit in the differential diagnosis of adenoid cystic carcinoma from polymorphous low-grade adenocarcinoma. *Oral Oncol*. 2007;43:67–76.
- Prasad AR, Saveria AT, Gown AM, et al. The myoepithelial immunophenotype in 135 benign and malignant salivary gland tumors other than pleomorphic adenoma. *Arch Pathol Lab Med*. 1999;123:801–6.
- Araujo V, Sousa S, Jaeger M, et al. Characterization of the cellular component of polymorphous low-grade adenocarcinoma by immunohistochemistry and electron microscopy. *Oral Oncol*. 1999;35:164–72.
- Prasad ML, Barbacioru CC, Rawal YB, et al. Hierarchical cluster analysis of myoepithelial/basal cell markers in adenoid cystic carcinoma and polymorphous low-grade adenocarcinoma. *Mod Pathol*. 2008;21:105–14.
- Crum CP, McKeon FD. P63 in epithelial survival, germ cell surveillance, and neoplasia. *Ann Rev Pathol*. 2010;5:349–71.
- Edwards PC, Bhuiya T, Kelsch RD. Assessment of p63 expression in the salivary gland neoplasms adenoid cystic carcinoma, polymorphous low-grade adenocarcinoma, and basal cell and

- canalicular adenomas. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 2004;97:613–9.
26. Foschini MP, Gaiba A, Cocchi R, et al. p63 expression in salivary gland tumors: role of DeltaNp73L in neoplastic transformation. *Int J Surg Pathol.* 2005;13:329–35.
 27. Park CK, Oh YH. Expression of p63 in reactive hyperplasias and malignant lymphomas. *J Korean Med Sci.* 2005;20:752–8.
 28. Fukushima N, Satoh T, Sueoka N, et al. Clinico-pathological characteristics of p63 expression in B-cell lymphoma. *Cancer Sci.* 2006;97:1050–5.
 29. Bishop JA, Teruya-Feldstein J, Westra WH, et al. p40 (DeltaNp63) is superior to p63 for the diagnosis of pulmonary squamous cell carcinoma. *Mod Pathol.* 2012;25:405–15.
 30. Bishop JA, Montgomery EA, Westra WH. Use of p40 and p63 immunohistochemistry and human papillomavirus testing as ancillary tools for the recognition of head and neck sarcomatoid carcinoma and its distinction from benign and malignant mesenchymal processes. *Am J Surg Pathol.* 2014;38:257–64.
 31. Tilson MP, Bishop JA. Utility of p40 in the differential diagnosis of small round blue cell tumors of the sinonasal tract. *Head Neck Pathol.* 2014;8:141–5.
 32. Pelosi G, Fabbri A, Rossi G, et al. A two-hit minimalist diagnostic algorithm based on p40 (deltaNp63) and TTF-1 immunostaining upon small biopsy/cellblock samples for differentiating main subtypes of non-small cell lung cancer and sparing material. *J Thorac Oncol.* 2011;6:S335–6.
 33. Pogodzinski MS, Sabri AN, Lewis JE, et al. Retrospective study and review of polymorphous low-grade adenocarcinoma. *The Laryngoscope.* 2006;116:2145–9.
 34. Seethala RR, Johnson JT, Barnes EL, et al. Polymorphous low-grade adenocarcinoma: the University of Pittsburgh experience. *Arch Otolaryngol Head Neck Surg.* 2010;136:385–92.
 35. Lee SY, Kim BH, Choi EC. Nineteen-year oncologic outcomes and the benefit of elective neck dissection in salivary gland adenoid cystic carcinoma. *Head Neck.* 2013. doi:[10.1002/hed.23537](https://doi.org/10.1002/hed.23537).
 36. Skalova A, Simpson RH, Lehtonen H, et al. Assessment of proliferative activity using the MIB1 antibody help to distinguish polymorphous low grade adenocarcinoma from adenoid cystic carcinoma of salivary glands. *Pathol Res Pract.* 1997;193:695–703.
 37. Vargas H, Sudilovsky D, Kaplan MJ, et al. Mixed tumor, polymorphous low-grade adenocarcinoma and adenoid cystic carcinoma of the salivary gland. Pathogenic implications and differential diagnosis by Ki-67 (MIB1), BCL2, and S-100 immunohistochemistry. *Appl Immunohistochem.* 1997;5:8–16.
 38. Lazzaro B, Cleveland D. P53 and Ki-67 antigen expression in small oral biopsy specimens of salivary gland tumors. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 2000;89:613–7.
 39. de Araujo VC, Passador-Santos F, Turssi C, et al. Polymorphous low-grade adenocarcinoma: an analysis of epidemiological studies and hints for pathologists. *Diagn Pathol.* 2013;8:6.