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Verrucous carcinoma of the esophagus: improvement of diagnosis and prognosis

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Abstract

Verrucous carcinoma of the esophagus (VCE) is a special variant form of esophageal squamous cell carcinoma. VCE presents a unique superficial growth pattern that is characterized as an exophytic, slow-growing mass. We reviewed previous reports of the 56 cases and divided them into two groups: from 1967 to 1999 (19 cases; the former period) and from 2000 to 2020 (37 cases; the latter period) to compare the diagnosis and prognosis of VCE. Patients with T4 disease tended to be higher in 6 (32%) of the19 cases in the former period. On the other hand, T1 and T2 diseases were high in 23 (62%) and T4 was very low; only 2 (5%) of the 37 cases in the latter period. It is presumed that surveillance by endoscopic examination has become common, as the risk factors and characteristic appearances of VCE are well known. Moreover, improvements in surgical procedures and perioperative management in recent years has been related to the favorable prognoses in the latter period. Since reports in the literature have stated that chemotherapy and radiotherapy might be inadequate as means of curative therapy, esophagectomy should be recommended as curative treatment because of VCE's low potential for lymph node and distant organ metastasis.

Introduction

Verrucous carcinoma of the esophagus (VCE) is a special variant form of esophageal squamous cell carcinoma. In 1967, Minielly et al. reported five cases of VCE for the first time[1]. VCE is slow-growing, well-differentiated squamous cell malignancy associated with nodular, papillary, and wart-like appearance. VCE is often difficult to diagnose before surgical excision, because in most cases, the superficial layer of the tumor is covered by non-malignant tissue[2]. Because of the paucity of cases, therapeutic strategies have not been well assessed. In this mini review we reviewed previous reports and discussed VCE.

Characteristics of verrucous carcinoma

We searched the literature that reported VCE using the keywords "esophagus" and "verrucous carcinoma" in the PubMed database during the period from 1967 to 2020 (Table 1). There were only 56 cases that has discussed VCE (including our case). Although males have predominated, the proportion of women has been higher in VCE patients (35 males, 19 females, 2 gender unknown) than that in conventional esophageal squamous cell carcinoma patients. Age has been as same as those of esophageal squamous cell carcinoma patients (median, 63 years; range, 36-79 years). Dysphagia was the most common chief complaint (47 (84%) of the 56 cases). The tumors have been predominantly located at the lower third of the

Table 1: Reported cases of Verrucous carcinoma of the esophagus

No	Author	Year	Age/Sex	Location	1st diagnosis	Pre Tx.[a] diagnosis	Tumor size (cm)	Treatment	Prognosis	T	N	M
1	Minielly[1]	1967	58/M	upper	benign	VC (Bx.[b] 3 times)	9×8.5	OPE[c]	1m dead	3	0	0
2		1967	70/F	upper	VC[d]	VC	large tumor	RT[e]	N/A[f]	N/A	N/A	N/A
3		1967	70/F	upper	VC	VC	large tumor	RT	2m dead	4	N/A	N/A
4		1967	36/M	lower	SCC[g]	SCC	9×8	OPE	2m dead	4	+	N/A
5		1967	57/M	lower	benign	VC (Bx. 2 times)	N/A	BSC[h]	5m dead	N/A	N/A	N/A
6	Parkinson[13]	1970	76/M	middle	SCC	SCC	7.5	BSC	1m dead	1b	0	0
7	Meyerowitz[14]	1971	45/M	lower	benign	benign	8×5.5	OPE, RT	9m dead	2	N/A	0
8	Sridher[15]	1980	54/M	lower	benign	benign	2	OPE	N/A	1b	0	N/A
9	Sakurai[5]	1983	78/M	upper	VC	VC	10×5	CT[i]	6m alive	4	N/A	N/A
10	Agha[16]	1984	66/M	upper	VC	VC	large tumor	BSC	2m dead	4	N/A	N/A
11	Barbier[17]	1987	50/F	lower	VC	VC	N/A	OPE	10m alive	1a	0	0
12	Koerfgen[18]	1988	75/M	lower	benign	SCC (Bx. repeatedly)	N/A	OPE	36m alive	2	0	0
13		1988	54/ unknown	lower	benign	SCC (Bx. repeatedly)	6.5×6.5	OPE	18m alive	2	0	0
14	Jasim[2]	1990	79/M	lower	benign	benign	9×6	BSC	dead	N/A	0	0
15	Biemond[6]	1991	76/F	middle	benign	benign	15	BSC	1m dead	4	0	0
16	Roach[19]	1993	67/M	upper	benign	VC (Bx. repeatedly)	7	BSC	2m dead	4	0	0
17	Garrard[20]	1994	51/F	middle	VC	VC	10	OPE	9m alive	2	0	0
18	Kavin[3]	1996	76/unknown	lower	benign	benign	N/A	BSC	1m dead	N/A	+	N/A
19	Malik[21]	1996	66/M	lower	benign	benign	5×2	OPE	36m alive	2	0	0
20	Tajiri[22]	2000	40/M	lower	VC	VC	0.6×0.8	EMR[j]	48m alive	1a	0	0
21	Ereno[23]	2001	65/F	middle	N/A	N/A	11	OPE	N/A	N/A	N/A	N/A
22	Osborn[24]	2003	67/M	lower	benign	benign	8×8	OPE	9m alive	2	0	0
23	Devlin[7]	2004	56/F	lower	benign	VC (Bx. 5 times)	2.7	OPE	14m alive	1b	0	0
24	Pfitzmann[25]	2004	66/F	lower	N/A	N/A	N/A	OPE	N/A	N/A	N/A	N/A
25	Liberale[26]	2005	41/M	lower	VC	VC	N/A	Antiviral Tx.	6m dead	4	N/A	N/A
26	Petris[27]	2005	73/M	lower	benign	benign	N/A	OPE	N/A	3	0	0
27		2005	58/M	lower	benign	benign	6×5.5	OPE	N/A	3	0	0
28	Na[28]	2009	50/M	middle	benign	VC (Bx. 5 times)	7.5×4.8	OPE	6m alive	2	0	0
29	Oh[8]	2009	73/F	upper	benign	VC (Bx. repeatedly)	3.5	BSC	23m alive	1a	0	0
30	Garcia[29]	2010	71/F	middle	benign	benign	3.9×2.5	OPE	N/A	2	0	0
31	Tonna[30]	2010	61/M	extensive	benign	benign	10	OPE	12m alive	1b	0	0
32	Munson[31]	2010	63/F	extensive	VC	VC	16	CRT[k]	N/A	3	+	0
33	Taniyama[32]	2012	74/M	middle	benign	SCC (Bx. 3 times)	5	OPE	6m alive	2	0	0
34	Vieira[33]	2013	58/M	N/A	benign	benign	N/A	OPE	1m dead	2	0	0
35	Ahmed[34]	2013	58/F	middle-lower	VC	VC	N/A	OPE, CRT	N/A	N/A	N/A	N/A
36	Sweetser[35]	2014	61/M	extensive	N/A	N/A	N/A	OPE, CRT	72m alive	2	0	0
37		2014	73/F	lower	N/A	N/A	N/A	CRT	36m alive	N/A	N/A	N/A
38		2014	66/M	lower	N/A	N/A	N/A	OPE	120m alive	1	0	0
39		2014	70/F	extensive	N/A	N/A	N/A	OPE	6m dead	1	0	0
40		2014	71/M	middle	N/A	N/A	N/A	N/A	36m dead	2	0	0
41		2014	57/M	lower	N/A	N/A	N/A	N/A	N/A	3	0	0
42		2014	75/F	lower	N/A	N/A	N/A	N/A	N/A	1	0	0
43		2014	62/M	extensive	N/A	N/A	N/A	OPE	96m alive	3	0	0
44		2014	63/F	extensive	N/A	N/A	N/A	CRT	12m alive	3	0	0
45		2014	68/M	extensive	N/A	N/A	N/A	OPE, CRT	24m alive	1	0	0
46		2014	62/F	middle	N/A	N/A	N/A	OPE	24m alive	1	0	0
47	Behrens[36]	2014	77/M	extensive	benign	VC (Bx. 2 times)	9	EMR	84m alive	1a	0	0
48	Ramani[37]	2014	78/M	middle-lower	benign	VC (Bx. repeatedly)	5	CRT	N/A	4	+	0

49	Brandalise[38]	2015	64/M	extensive	benign	benign	16	OPE, RT	12m alive	3	0	0
50	Abe[39]	2016	68/M	lower	benign	benign	1	ESD[l]	N/A	1a	0	0
51	Egeland[40]	2016	67/M	lower	benign	benign	N/A	OPE	N/A	2	0	0
52		2016	59/M	N/A	benign	benign	N/A	OPE	N/A	2	0	0
53	Cox[41]	2017	62/M	middle	SCC	SCC	9.5	OPE	N/A	1b	0	0
54	Hoffmann[42]	2018	61/M	lower	VC	VC	N/A	OPE	24m alive	1b	0	0
55		2018	52/F	lower	VC	VC	10	OPE	24m alive	2	0	0
56	Tabuchi[43]	2020	56/F	lower	benign	SCC (Bx. 6 times)	12	OPE	96m alive	3	0	0

Tx.[a]: Treatment; Bx.[b]: Biopsy; OPE[c]: Operation; VC[d]: Verrucous carcinoma; RT[e]: Irradiation; N/A[f]: Not applicable; SCC[g]: Squamous cell carcinoma; BSC[h]: Best supportive care; CT[i]: Chemotherapy; EMR[j]: Endoscopic mucosal resection; CRT[k]: Chemoradiation therapy; ESD[l]: Endoscopic submucosal dissection

esophagus (37 cases, 66%), and this frequent location in the lower-third of the esophagus has suggested that VCE might be associated with chronic inflammation of esophageal mucosa[3].

Although tumor sizes of VCE have been large, depth of invasion has been shallow. In 27 (82%) of the 33 cases in which tumor size was recorded, the tumor measured 5 cm or more in diameter. Tumor invasion has been limited to the muscle layer (T1: 16 cases and T2: 15cases): in 65% of the patients in which depth of tumor invasion was recorded, but in seventeen cases (35%) the tumor was locally advanced (T3: 9 cases and T4: 8 cases). In addition, lymph node metastasis (9%) and distant organ metastasis (0%) have occurred very low and these findings were considered as special features of VCE.

Treatment consisted of surgery in 34 cases, chemoradiation therapy in 7 cases, radiotherapy in 4 cases, chemotherapy in 1 case, and best supportive care in 8 cases. The effectiveness of both chemotherapeutic regimens and radiotherapy that was used to treat conventional squamous cell carcinoma has been very limited for VCE[4,5]. If the surgery is technically possible to perform, esophageal resection should be considered even in a locally advanced VCE, because VCE has very low incidence of lymph node metastases and the limited sensitivity of chemotherapy and radiotherapy.

Comparison of diagnosis and prognosis of VCE according to the era

Histopathological diagnosis

We divided the literature reports into two groups: from 1967 to 1999 (19 cases; the former period) and from 2000 to 2020 (37 cases; the latter period), and compared the diagnosis and prognosis of VCE (Table.2). Despite the unique characteristic findings, it is difficult to make a definitive diagnosis of VCE because superficial biopsies tend to show only nonspecific acanthosis, parakeratosis, or hyperkeratosis, with associated acute and chronic inflammation. A deeper and full-thickness biopsy or a fully resected specimen is often needed to differentiate VCE from benign lesions[6,7]. The histological picture of VCE and

Table 2: Comparison of diagnosis and prognosis of VCE according to the era

	Former period (n=19) (1967-1999)	Latter period (n=37) (2000-2020)
1st diagnosis		
Benign	11	17
VC[a] or SCC[b]	8	7
Unknown	0	13
Pre Tx.[c] diagnosis		
Benign	6	10
VC or SCC	13	14
Unknown	0	13
T		
1	3	13
2	5	10
3	1	8
4	6	2
Unknown	4	4
N		
(−)	11	30
(+)	2	2
Unknown	6	5
M		
(−)	11	32
(+)	0	0
Unknown	8	5
Treatment		
OPE[d]	9	25
EMR[e] or ESD[f]	0	3
CRTg	0	4
RT[h]	2	0
CT[i]	1	0
Antiviral Tx.	0	1
BSC[j]	7	1
Unknown	0	3
Prognosis		
Dead	11	4
Alive	6	19
Unknown	2	14

VC[a]: Verrucous carcinoma; SCC[b]: Squamous cell carcinoma; Tx.[c]: Treatment; OPE[d]: Operation; EMR[e]: Endoscopic mucosal resection; ESD[f]: Endoscopic submucosal dissection; CRTg: Chemoradiation therapy; RT[h]: Irradiation; CT[i]: Chemotherapy; BSC[j]: Best supportive care

benign squamous cell papilloma is very similar. However, VCE tends to grow deeply and invasively, whereas benign squamous papilloma tends to grow superficially. Biemond et al.[6] proposed that the histopathological findings of invasion were essential to differentiate VCE from benign squamous papilloma. It is very important to know that benign squamous papilloma sometimes shows no invasions, but dysplastic changes. In fact, only 15 (27%) of the 56 cases were diagnosed as esophageal VC or SCC based on the first biopsy pathology findings. In addition, 28 (50%) of the 56 cases were diagnosed as benign lesions by the first biopsy, and they were subjected to endoscopic biopsy many times in order to make a definitive diagnosis. However, in 16 (57%) of these 28cases, pre-treatment diagnosis were still benign lesions though repeated endoscopic biopsies, consequently diagnosis of malignancy could not be made before surgery or autopsy. The rates of accurate histopathological diagnosis have not changed between the two periods. Difficulty in the histopathological diagnosis from the biopsy specimen may be related to these lower accuracy rate, because differential diagnosis of VCE can usually be achieved by histological evaluation of surgically or endoscopically resected specimens[8].

Tumor staging

Regarding T factors, patients with T4 disease tended to be higher in 6 (32%) of the19 cases in the former period. On the other hand, T1 and T2 were high in 23 (62%) and T4 was very low; only 2 (5%) of the 37 cases in the latter period. Since the ability of histopathological diagnosis might be equal between the former period and the latter period, these differences in the depth of tumor invasion might be affected by improvement in diagnostic imaging equipment such as CT, MRI, and endoscopy. In addition to the classic risk factors such as heavy consumption of nicotine and alcohol, VCE is significantly associated with chronic inflammation of esophageal mucosa. Almost all patients had affected the medical histories that were typically associated with esophageal injury or chronic inflammation: achalasia, reflux esophagitis, candida esophagitis, and heavy consumption of nicotine and alcohol were found in 90% of the patients before the diagnosis of VCE[3]. Therefore, it is presumed that surveillance by endoscopic examination has become common that can detect the tumor in early stage, as the risk factors and characteristics appearances of the VCE are well known. Moreover, using EUS may provide information that is crucial to the diagnostic process[7]. Inflammatory histopathologic findings that extend deeper into the submucosa and the muscularis propria have been found in the majority of VCE. Since EUS enables to visualize the distorted architecture and local invasion of VCE, it is considered that EUS is ideally suited to detect these impressive changes in the esophageal wall and to establish the appropriate diagnosis of VCE.

Lymph node and distant metastases are known to be extremely rare. N factor did not change with time and lymph node metastasis tended to be less. Patient with positive lymph node metastasis was very low; in 2 (11%) of the19 cases in the former period and in 2 (5%) of the 37 cases in the latter period. There were no distant organ metastases in both the former period and the latter period. The reason why lymph node or distant metastasis is very limited is speculated that dysplasia of tumor cells is weak and alveolar nest formation is poor in the VCE tissues, as can be seen from the fact that it is difficult to distinguish it from a benign disease in pathological findings.

Treatment and prognosis

In the former period, treatment consisted of surgery in 9 cases (47%), radiotherapy in 2 cases (11%), chemotherapy in 1 case (5%), and best supportive care (BSC) in 7 cases (37%). On the other hands, in the latter period, treatment consisted of surgery in 25 cases (68%), endoscopic resection in 3 cases (8%), chemoradiation therapy in 4 cases (11%), antiviral treatment in 1 case (3%), and BSC in 1 case (3%). Among the documents that described the prognosis, 11(65%) of the 17 cases died in the former period, but only 4 (17%) of the 23 cases died in the latter period. In the former period, BSC was selected as a treatment in 7 (37%) of 19 cases, and tumor progression due to delay in diagnosis was suggested to be related to this high rate of immediate patient death. In the latter period, tumor resections including surgery and endoscopic resection were performed in the three quarters of patients. It is considered that these favorable prognoses in the latter period are due to the full understanding of the characteristics of VCE and the advancement in the imaging diagnosis, enabling early detection. Moreover, improvements in surgical procedures and perioperative management in recent years has been related to the favorable prognoses in the latter period as well as the low malignant potentials of VCE.

VCE patients uniformly respond well to surgical excision, if they are diagnosed before invasion of surrounding organs. Metastasis by VCE is exceptionally rare[9,10]. The effectiveness of radiotherapy and chemotherapy has been very limited[4]. There has been only one report that could demonstrate the partial therapeutic response with bleomycin[7]. Gothals et al.[9] and Kraus et al.[10] have both demonstrated that radiation is ineffective. Radiotherapy appears to be associated with poor outcomes, because it tends to be followed by recurrence and early metastasis with anaplastic transformation. Therefore, chemoradiotherapy cannot become a treatment option for VCE.

Recent studies have suspected that human papillomavirus (HPV) infection may be involved in carcinogenesis of VCE[11]. There are several reports of HPV-positive VCE cases[12]. It could be proposed that antiviral

treatment therapy might be a promising treatment for HPV-positive VCE and administration of HPV vaccine against VCE might prevent the acceleration of malignant progression.

Conclusions

The prognosis of VCE has improved recently, probably as the risk factors and characteristics appearances of the VCE have been well investigated. Esophagectomy should be recommended as curative treatment because of VCE's low potential for metastasis and the limited effectiveness of chemotherapy and radiotherapy.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

References

1. Minielly JA, Harrison EG Jr, Fontana RS, et al. Verrucous squamous cell carcinoma of the esophagus. Cancer. 1967; 20: 2078-87.
2. Jasim KA, Bareson MC. Verrucous carcinoma of the oesophagus-a diagnostic problem. Histopathology. 1990; 17(5): 473-5.
3. Kavin H, Yaremko L, Valaitis J, et al. Chronic esophagitis evolving to verrucous squamous cell carcinoma: possible role of exogenous chemical carcinogens. Gastroenterology. 1996; 110(3): 904-14.
4. Ferlito A, Rinaldo A, Mannara GM. Is primary radiotherapy an appropriate option for the treatment of verrucous carcinoma of the head and neck? J Laryngol Otol. 1998; 112: 132-9.
5. Sakurai T, Fuchigami T, Omae T, et al. Bleomycin in verrucous squamous cell carcinoma of the esophagus. Postgrad Med J. 1983; 59: 578-80.
6. Biemond P, ten Kate FJ, van Blankenstein M. Esophageal verrucous carcinoma: histologically a low-grade malignancy but clinically a fatal disease. J Clin Gastroenterol. 1991; 13(1): 102-7.
7. Devlin S, Falck V, Urbanski SJ, et al. Verrucous carcinoma of the esophagus eluding multiple sets of endoscopic biopsies and endoscopic ultrasound: a case report and review of the literature. Can J Gastroenterol. 2004 ul; 18(7): 459-62.
8. Oh K, Nishigami T, Takubo K, et al. A case of verrucous squamous cell carcinoma of the esophagus. Esophagus. 2009; 6(4): 263-7.
9. Gothals PL, Hnison EG, Devine KD. Verrucous squamous carcinoma of the oral cavity. Am J Surg. 1963; 106: 845-51.
10. Kraus FT, Perez-Mesa C. Verrucous carcinoma; Clinical and pathologic study of 105 cases involving oral cavity, larynx and genitalia. Cancer. 1966; 19(1): 26-38.
11. Chung CH, Gillison ML. Human papillomavirus in head and neck cancer: its role in pathogenesis and clinical implications. Clin Cancer Res. 2009; 15: 6758-62.
12. Tabuchi S, Koyanagi K, Ozawa S, et al. Verrucous carcinoma of the esophagus: its unique etiology and human papilloma virus. J Cancer Immunol. 2020; 2(2): 44-51.
13. Parkinson AT, Haidak GL, McInerney RP. Verrucous squamous cell carcinoma of the esophagus following lye stricture. Chest. 1970; 57(5): 489-92.
14. Meyerowitz BR, Shea LT. The natural history of squamous verrucose carcinoma of the esophagus. J Thorac Cardiovasc Surg. 1971; 61(4): 646-9.
15. Sridhar C, Zeskind HJ, Rising JA. Verrucous squamous-cell carcinoma: an unusual tumor of the esophagus. Radiology. 1980; 136: 614.
16. Agha FP, Weatherbee L, Sams JS. Verrucous carcinoma of the esophagus. Am J Gastroenterol. 1984; 79(11): 844-9.
17. Barbier PA, Luder PJ, Wagner HE, et al. Verrucous acanthosis—so-called verrucous carcinoma—of the esophagus. Z Gastroenterol. 1987; 25(2):93-7.
18. Koerfgen HP, Husemann B, Giedl J, et al. Verrucous carcinoma of the esophagus. Endoscopy. 1988; 20(6): 326-9.
19. Roach E, Barr G. Verrucous carcinoma of the oesophagus and achalasia. J Gastroenterol Hepatol. 1993; 8(1): 107-9.
20. Garrard CL, Sheih WJ, Cohn RA, et al. Verrucous carcinoma of the esophagus: surgical treatment for an often fatal disease. Am Surg. 1994; 60(8): 613-6.
21. Malik AB, Bidani JA, Rich HG, et al. Long-term survival in a patient with verrucous carcinoma of the esophagus. Am J Gastroenterol. 1996; 91(5): 1031-3.
22. Tajiri H, Muto M, Boku N, et al. Verrucous carcinoma of the esophagus completely resected by endoscopy. Am J Gastroenterol. 2000; 95(4): 1076-7.
23. Ereño C, Lopez JI, Loizate A, et al. Verrucous carcinoma of the esophagus. Endoscopy. 2001; 33(3): 297.
24. Osborn NK, Keate RF, Trastek VF, et al. Verrucous carcinoma of the esophagus: clinicopathophysiologic features and treatment of a rare entity. Dig Dis Sci. 2003; 48(3): 465-74.
25. Pfitzmann R, Abou-Rebyeh H, Krenn V, et al. Verrucous carcinoma of the esophagus - a rare entity. Zentralbl Chir. 2004 Jan; 129(1): 70-2.
26. Liberale G, De Simone P, Snoeck R, et al. Verrucous carcinoma of the esophagus. A case report. Minerva Chir. 2005; 60(1): 61-5.
27. De Petris G, Lewin M, Shoji T. Carcinoma cuniculatum of the esophagus. Ann Diagn Pathol. 2005; 9: 134-8.
28. Na S, Choi KD, Yoo C, et al. Verrucous carcinoma of the esophagus. 2004; 18: 459-62.
29. Garcia M, Lesquereux LM, Fernandez B, et al. Verrucous carcinoma of the esophagus: a complex diagnosis. Endoscopy. 2010; 42: E137–8.
30. Tonna J, Palefsky JM, Rabban J, et al. Esophageal verrucous carcinoma arising from hyperkeratotic plaques associated with human papilloma virus type 51. Dis Esophagus. 2010; 23(5): E17-20.
31. Munson GW, Romero Y, Francis DL. Verrucous squamous cell carcinoma: a rare esophageal malignancy. Clin Gastroenterol Hepatol. 2010; 8(6): A20.
32. Taniyama Y, Fujishima F, Takubo K, et al. A case of verrucous carcinoma of the esophagus associated with difficult histopathological diagnosis of endoscopic biopsy specimens. Esophagus. 2012; 9: 223–7.
33. Vieira CL, Lopes JC, Velosa J. A case of esophageal squamous cell carcinoma with positive HPV 11. Gastroenterol Hepatol. 2013; 36: 311-5.
34. Ahmed K, Timmerman G, Meyer R, et al. Verrucous carcinoma of the esophagus: a potential diagnostic dilemma. Case Rep Gastroenterol. 2013; 7: 498-502.
35. Sweetser S, Jacobs NL, Wong Kee Song LM. Endoscopic diagnosis and treatment of esophageal verrucous squamous cell cancer. Dis Esophagus. 2014; 27(5): 452-6.
36. Behrens A, Stolte M, Pech O, et al. Verrucous oesophageal carcinoma: single case report and case series including 15 patients-issues for consideration of therapeutic strategies. Viszeralmedizin. 2014; 30: 346-52.

37. Ramani C, Shah N, Nathan RS. Verrucous carcinoma of the esophagus: a case report and literature review. World J Clin Cases. 2014; 2(7): 284-8.

38. Brandalise A, Lorenzetti C, Aranha NC, et al. Verrucous carcinoma of the esophagus involving the entire esophagus. Atq Bras Cir Dig. 2015; 28(4): 293-4.

39. Abe T, Kato M, Itagaki M, et al. Endoscopic submucosal dissection for an atypical small verrucous carcinoma: a case report. J Med Case Rep. 2016; 10: 74.

40. Egeland C, Achiam MP, Federspiel B, et al. Verrucous squamous cell cancer in the esophagus: an obscure diagnosis. Case Rep Gastroenterol. 2016; 10: 466-71.

41. Cox R, Welch C, Cameron D, et al. Gastrointestinal: Verrucous cell carcinoma (VCC) of the esophagus: a rare variant of esophageal squamous cell carcinoma (SCC). J Gastroenterol Hepatol. 2017; 32: 544.

42. Hoffmann R, Hebenstreit A, Game PA, et al. Verrucous carcinoma of the oesophagus. ANZ J Surg. 2018; 88(11): E797–8.

43. Tabuchi S, Koyanagi K, Nagata K, et al. Verrucous carcinoma of the esophagus: a case report and literature review. Surg Case Rep. 2020; 6(1): 35.