Nayara Araújo Cardoso
Renan Rhonalty Rocha
Maria Vitória Laurindo
(Organizadores)

NOVOS PARADIGMAS DE ABORDAGEM NA **MEDICINA ATUAL 2**

Atena Editora
Ano 2019

Nayara Araújo Cardoso
Renan Rhonalty Rocha
Maria Vitória Laurindo
(Organizadores)

Novos Paradigmas de Abordagem na Medicina Atual 2

Atena Editora
2019

2019 *by Atena Editora*

Editora Executiva: Profª Drª Antonella Carvalho de Oliveira
Diagramação: Karine de Lima
Edição de Arte: Lorena Prestes
Revisão: Os Autores

Atena Editora
Ano 2019

Dados Internacionais de Catalogação na Publicação (CIP)
(eDOC BRASIL, Belo Horizonte/MG)

N945 Novos paradigmas de abordagem na medicina atual 2 [recurso eletrônico] / Organizadores Nayara Araújo Cardoso, Renan Rhonalty Rocha. – Ponta Grossa, PR: Atena Editora, 2019. – (Novos Paradigmas de Abordagem na Medicina Atual; v. 2)

Formato: PDF
Requisitos de sistema: Adobe Acrobat Reader
Modo de acesso: World Wide Web
Inclui bibliografia
ISBN 978-85-7247-414-6
DOI 10.22533/at.ed.146192006

1. Medicina – Pesquisa – Brasil. 2. Pesquisa médica. I. Cardoso, Nayara Araújo. II. Rocha, Renan Rhonalty. III. Série.
CDD 610.9

Elaborado por Maurício Amormino Júnior – CRB6/2422

Atena Editora
Ponta Grossa – Paraná - Brasil
www.atenaeditora.com.br
contato@atenaeditora.com.br

Atena Editora
Ano 2019

APRESENTAÇÃO

A obra “Novos Paradigmas de Abordagem na Medicina Atual” é integrada por uma série de livros de publicação da Atena Editora, em seus 18 capítulos do volume 2, a qual apresenta dados descritivos e epidemiológicos de doenças emergentes e reemergentes e a atuação dos profissionais da saúde sobre estas.

Nos últimos anos têm sido reconhecidas diversas infecções humanas até então desconhecidas, bem como a reemergência de outras que, ao longo dos anos, haviam sido controladas. As doenças emergentes são as que se desenvolvem com impacto significativo sobre o ser humano, por conta de sua gravidade, da alta probabilidade em acometer órgãos e sistemas principais e da potencialidade de deixar sequelas limitadoras e mesmo morte.

Dentre os fatores que contribuem para o reaparecimento de doenças reemergentes, como a sífilis e a Doença de Chagas, e o desenvolvimento de novas patologias, como microcefalia e variados tipos de câncer, estão os mecanismos de mutação e recombinação genéticas, demografia e comportamentos humanos, mudanças ecológicas, uso inapropriado das tecnologias em saúde e a decadência dos sistemas de saúde, fruto da elevada demanda e dos custos crescentes da assistência médica, que vem a absorver grande parte dos recursos, antes destinados às áreas de prevenção e controle de agravos. Assim, medidas como a potencialização da comunicação e informação em saúde pública e das práticas preventivas em saúde, implantação de políticas de uso racional de medicamentos, estímulo a mudanças no estilo de vida e equilíbrio com a natureza contribuem na prevenção do aparecimento dessas patologias.

Assim, esta obra é dedicada tanto para os estudantes e profissionais da área da saúde, quanto para a população de forma geral e aborda os seguintes temas: fatores epidemiológicos da Doença de Chagas; correlação entre alterações socioambientais e surgimentos de doenças; novos vetores de propagação de doença bacteriana; patologias relacionadas às alterações genéticas; aspectos relacionados à microcefalia; drogas de abuso como problema de saúde pública; fatores relacionados à subnotificação de sífilis; relatos de casos sobre padrões de diferentes neoplasias, entre outros.

Sendo assim, almejamos que esta obra colabore com os profissionais de saúde, atualizando os conhecimentos destes sobre algumas patologias emergentes e reemergentes e assim, norteie o desenvolvimento de estratégias de prevenção e paralelamente embase o tratamento e manejo dos casos já existentes.

Nayara Araújo Cardoso
Renan Rhonalty Rocha

SUMÁRIO

CAPÍTULO 16

PRIMARY NEUROENDOCRINE NEOPLASM OF THE ESOPHAGUS – REPORT OF 14 CASES FROM A SINGLE INSTITUTE AND REVIEW OF THE LITERATURE

Francisco Tustumi
Faculdade de Medicina da Universidade de São Paulo, São Paulo

Rodrigo Hideki Uema
Faculdade de Medicina da Universidade de São Paulo, São Paulo

Flavio Roberto Takeda
Instituto do Cancer do Estado de Sao Paulo (ICESP), São Paulo

Guilherme Luiz Stelko Pereira
Instituto do Cancer do Estado de Sao Paulo (ICESP), São Paulo

Ulysses Ribeiro Junior
Instituto do Cancer do Estado de Sao Paulo (ICESP), São Paulo

Rubens Antônio Aissar Sallum
Faculdade de Medicina da Universidade de São Paulo, São Paulo

Ivan Cecconello
Faculdade de Medicina da Universidade de São Paulo, São Paulo

ABSTRACT: Context: Most prevalent esophageal neoplasm is squamous cell carcinoma and adenocarcinoma. Other tumors are uncommon and poorly studied. Primary neuroendocrine esophageal neoplasm is a rare carcinoma and most of its therapy management is based on lung neuroendocrine studies. Neuroendocrine tumors can be clustered in the following subtypes: high grade (small cell carcinoma or large cell carcinoma) and low grade (carcinoids). **Objectives:** The present study aims to assess clinical and pathological neuroendocrine esophageal tumors in a single oncologic center. **Methods:** A retrospective analysis of patients and review of the literatures was performed. Fourteen patients were identified as neuroendocrine tumors, 11 male and 3 female patients. Mean age was 67.3 years old. Ten patients were classified as small cell, 3 as large cell and 1 as carcinoid. Four patients presented squamous cell carcinoma simultaneously and 1 also presented adenocarcinoma. Main sites of metastasis were liver, peritoneum, lung and bones. Most patients died before 2 years of follow-up. Patient with longer survival died at 35 months after diagnosis. **Conclusions:** Neuroendocrine esophageal tumors are rare; affect mainly men in their sixties or seventies. High grade tumors can be mixed to other subtypes neoplasms, such as adenocarcinoma and squamous cell carcinoma. Most of these patients have poor overall survival rates.

KEYWORDS: Neuroendocrine tumors, Esophageal neoplasms, Small cell carcinoma, Carcinoid tumor

NEOPLASIA NEUROENDÓCRINA DE ESÔFAGO – RELATO DE 14 CASOS EM UM CENTRO ONCOLÓGICO E REVISÃO DA

RESUMO: Introdução: As neoplasias esofágicas mais prevalentes são o adenocarcinoma e o carcinoma espinocelular. Outros subtipos histológicos são incomuns e pouco estudados. Neoplasia neuroendócrina esofágica é uma patologia rara e seu manejo atualmente se baseia nos conhecimentos prévios de tumores neuroendócrinos de pulmão. Tumores neuroendócrinos podem ser divididos nas seguintes formas: alto grau (pequenas células ou grandes célula) e baixo grau (carcinoides). **Objetivos:** Avaliar clinica e patologicamente os tumores de esôfago em um centro oncológico referenciado. **Métodos:** Foi realizada análise retrospectiva e revisão da literatura. Foram identificados 14 pacientes com tumores neuroendócrino, sendo 11 homens, 3 mulheres. Idade média foi de 67,3 anos de idade. Desses pacientes, 10 foram classificados como pequenas células, 3 como grandes células e 1 como carcinoide. Foram encontrados 4 casos de tumor misto neuroendócrino e carcinoma espinocelular, e 1 caso de tumor misto adenoneuroendócrino. Principal sítio de metástases foi fígado, peritônio, pulmão e ossos. A maioria dos pacientes foi a óbito em até 2 anos de seguimento. Paciente com sobrevida mais longa foi a óbito após 35 meses do diagnóstico. **Conclusões:** Neoplasias neuroendócrinas de esôfago são raras, afetam principalmente o sexo masculino na 7ª ou 8ª década de vida. A maioria dos pacientes com tumores de alto grau tem sobrevida curta.
PALAVRAS-CHAVE: Tumores de esôfago, carcinoide, tumor neuroendócrino

INTRODUCTION

Esophageal cancer is a rapidly progressive disease with poor survival rates. Most of these tumors are either adenocarcinoma or squamous cell carcinoma histologic types. Less frequent cancer subtypes, such as melanoma, lymphomas or neuroendocrine tumors are uncommon and poorly explored. [34]

Neuroendocrine esophageal neoplasms are rare and most of studies are case reports. The classification and nomenclature are not well established and knowledge acquired in neuroendocrine neoplasms of lungs and certain gastrointestinal sites, such as pancreas, usually guide esophageal neuroendocrine management.

Neuroendocrine neoplasm subtypes are grouped based upon shared neuroendocrine features. The subtypes comprise small cell carcinoma, large cell neuroendocrine carcinoma, typical carcinoid, and atypical carcinoid. [140]

This article is a descriptive report of clinical and pathological features of cases of neuroendocrine esophageal tumors in our institute, along 8 years of experience, and a review of the literature.

PATIENTS AND METHODS

All esophageal cancer patients' charts of our institution were reviewed, between 2008 and 2016. Cases of neuroendocrine neoplasm were identified and clinical and pathological features of these patients were assessed.

For review of the literature, database search was performed in MEDLINE, with search algorithm: ("neuroendocrine"[All Fields] OR "carcinoid tumor"[MeSH Terms] OR "carcinoid"[All Fields] OR "small cell carcinoma" [MeSH Terms] OR "large cell carcinoma") AND ("oesophagus"[All Fields] OR "esophagus"[All Fields] OR esophageal [All Fields]). Period searched up to 2016, with no idiom restriction. Review studies and no full-text studies were excluded. When more than one publication of a single trial existed, only the publication with the most complete data was included.

RESULTS

A total of 1,574 of esophageal cancers were reviewed. Fourteen (0.89%) cases of neuroendocrine neoplasm were selected, 3 female and 11 male patients (see table 1). Mean age was 67.3 (range 47 to 80) years old. Table 2 shows immunohistochemical panel of neuroendocrine neoplasm.

Patient	Age	Sex	KPS	ECOG	Stage	Histologic subtype	Associated neoplasm	Site	Survival (months)	Esophagectomy	Chemotherapy	Radiotheraphy
1	79	M	50	4	Unstaged	SCCE	No	Lower	2	No	No	No
2	65	M	90	1	IIIA	SCCE	No	Middle	Alive at 26 months	Yes	No	No
3	60	M	80	1	IIIB	LCCE	No	Middle and lower	13	No	IP	30 cGy
4	65	M	30	4	IA	Carcinoid	No	Lower	7	No	No	No
5	75	F	90	1	IIA	LCCE	No	Lower	13	Yes	IP, PC	45 cGy
6	51	M	100	0	IIIC	SCCE	No	Upper and middle	Lost to follow-up at 4 months	No	EP	No
7	58	M	80	2	IV	SCCE	SCC	Middle	2	No	No	No
8	64	M	100	0	IIIA	SCCE	SCC	Middle and lower	35	Yes	IP, PT	45 cGy
9	47	M	100	0	IV	SCCE	No	Lower	10	No	IP, PT	50.4 cGy
10	78	F	70	1	IV	SCCE	SCC	Lower	13	No	IP, PT	45 cGy
11	75	M	80	1	IIIC	SCCE	No	Upper and middle	12	No	IP	45 cGy
12	80	F	50	3	IV	SCCE	SCC	Middle	6	No	No	No
13	76	M	60	3	IV	SCCE	No	Middle	5	No	IP	No
14	69	M	90	1	IIIB	LCCE	EA	Lower	18	Yes	XP (neoadjuvant), IP	No

Table 1. *Main characteristics of the 14 patients diagnosed with neuroendocrine tumor. SCEC: Small cell esophageal cancer; LCEC: Large cell esophageal cancer. KPS: Karnofsky Performance Status; ECOG:Eastern Coorporative Oncology Group. SCC: Squamous Cell Carcinoma. EA: Esophageal adenocarcinoma. PC: Paclitaxel and Carboplatin. PT:Cisplatin and Paclitaxel.IP: Irinotecan and Cisplatin.EP: Etoposide and Cisplatin.XP: Capecitabine and*

Cisplatin.

8	Grade of cellular differentiation	Syp	CgA	Ki-67(%)	Ber-EP4	Ck7	AE-1/AE-3	35BH11	P63	CD 56	TTF-1	Vimentin
1	Poorly	Positive	NP	>90	NP	NP	NP	NP	NP	Positive	NP	NP
2	Poorly	NP	Negative	80-90	NP	NP	NP	Positive	Negative	Positive	Positive	NP
3	Poorly	NP	Positive	90	Positive	NP	Negative	NP	Negative	NP	NP	NP
4	Well	Positive	Positive	<1	NP	NP	NP	NP	NP	NP	NP	NP
5	Poorly	Positive	Positive	>90	NP	Positive	NP	NP	Negative	NP	NP	NP
6	Poorly	Positive	Positive	90	NP	NP	NP	NP	NP	NP	Positive	NP
7	Poorly	Positive	Positive	NP	Positive	NP	NP	NP	Positive	NP	NP	NP
8	Poorly	Negative	Positive	50	NP	Positive	Positive	NP	Positive	Positive	Positive	Positive
9	Poorly	Positive	Positive	80-90	NP	NP	NP	Positive	Negative	Positive	NP	NP
10	Poorly	Positive	Positive	NP	NP	Negative	Positive	Positive	Negative	Positive	Positive	NP
11	Poorly	NP	Negative	NP	Negative	NP	Positive	Positive	Negative	Positive	NP	NP
12	Poorly	Positive	Positive	90	NP	NP	Positive	NP	Positive	Positive	NP	NP
13	Poorly	NP	NP	NP	NP	NP	Positive	Positive	Positive	Positive	Positive	Positive
14	Poorly	Positive	Positive	70	Negative	Positive	NP	NP	Negative	NP	NP	NP

Table 2. Immunohistochemical panel of patients with esophageal neuroendocrine neoplasm.
Syp: Synaptophysin. CgA: Chromogranine A. Ck: Cytokeratin. NP: Not performed.

Three were classified as large cell esophageal carcinoma (LCEC), 10 as small cell carcinoma (SCEC), and 1 as carcinoid. Distal and middle esophagus were more often affected.

Endoscopic appearance was usually a vegetating and infiltrative tumor, except carcinoid subtype. See figure 1.

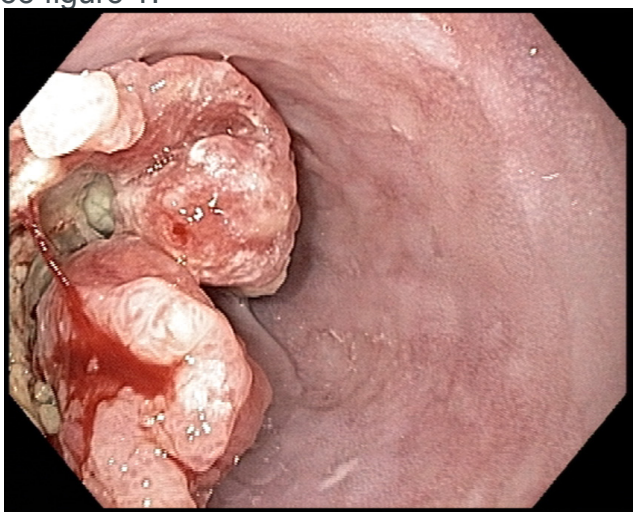

Figure 1. *Endoscopic view of a high grade neuroendocrine neoplasm. It shows a circumferential infiltrative and ulcerating tumor.*

Main symptoms were dysphagia (14/14) and weight loss (mean 11.7 ± Std Dev 6.3 kg). Duration of symptoms prior to diagnosis was 6.2 ± Std Dev 3.3 months.

Associated squamous cell carcinoma could be seen in 4/14 cases and associated adenocarcinoma (adenoneuroendocrine) in 1/14. Immunohistochemical panel can be seen in table 2.

Of these patients, 10/14 had previous history of high amount of alcohol intake and 12/14 were tobacco smokers.

Most cases were diagnosed at late stages (III and IV), accordingly AJCC 7th Edition. [122] Metastasis sites were lungs, liver, adrenal, peritoneal and bones.

Cause of death was pneumonia in 5 cases, urinary tract infection in 1 case, and sepsis of unknown origin in 1 case. The 5 remaining patients, cause of death was not clearly established.

Curative intent surgery was performed in 4/14 patients, of which one is still alive at 26 months of follow-up.

Most cases had low survival rates (see figure 2). Patient who lived longer died at 35 months of pneumonia. Patient "2" is still alive without disease up to this paper publication. Patients "6" lost to follow-up, with disease. The remaining patients died with disease.

Patient diagnosed with carcinoid tumor presented myelofibrosis during follow-up, leading to pancytopenia and early death.

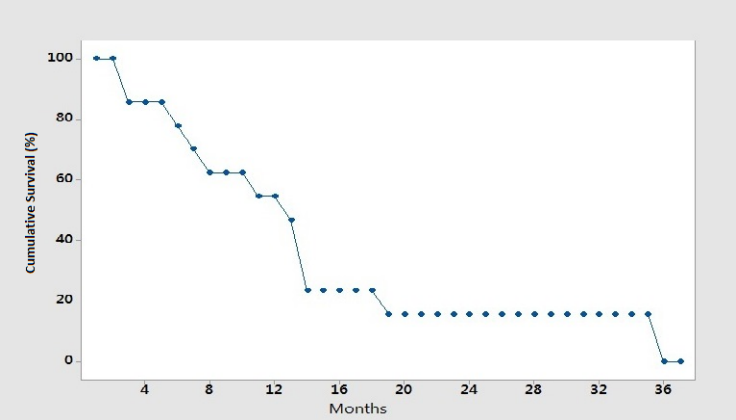

Figure 2. Kaplan-Meir curve for survival of patients with esophageal neuroendocrine neoplasm.

REVIEW OF THE LITERATURE

For review of the literature, a total number of articles by database search were 1007. After excluding duplicates and screening by title and abstract, 154 articles remained. [1-33, 35-79, 81-115, 117-119, 121, 123-139, 141-162]

A cumulative sample size of 2,957 patients was evaluated, in 20 different countries. Of this patients, 2,899 were SCEC (77% in East countries; 23% in West countries); 35 were LCEC (6% in East countries; 94% in West countries); and 23 were carcinoid (54% in East countries; 43% in West countries).

Among all esophageal malignances, prevalence of SCEC was 1.05% in East countries and 0.72% in West countries. There are few studies data concerning carcinoid tumors and LCEC prevalence. Most of the studies approaching LCEC were performed in West countries.

Neoplasms were staged as limited disease (LD) or extend disease (ED). LD is

defined as disease confined to the esophagus and adjacent organs with or without regional lymph node involvement while ED is defined for neoplasm with distant spread. [59] Main features and differences concerning neuroendocrine subtypes are presented in table 3.

		SCEC	%	LCEC	%	Carcinoid	%
Prevalence	East countries	1,527 (145,717)	1.048	Unknown	-	Unknown	-
	West countries	533 (73,290)	0.727	5 (1,105)	0.452	Unknown	-
Age	Mean	63.8	-	62.1	-	58.3	-
	< 60 yr	542	48.26	0	0	12	57.1
	≥ 60 yr	581	51.74	4	100	9	42.9
Sex	M	1,517	69.5	32	88.9	14	70
	F	666	30.5	4	11.1	6	30
Mixed	SCC	82 (786)	10.4	2 (36)	5.6	0 (13)	0
	Adenocarcinoma	31 (786)	4	14 (36)	38.9	0 (13)	0
Tumor site	Upper	202	12.4	1	10	1	7.7
	Middle	904	55.5	5	50	2	15,4
	Lower/GEJ	523	32.1	4	40	10	76.9
Stage	LD	1,519	70.2	16	55.2	13	100
	ED	645	29.8	13	44.8	0	0
Tumor size	< 5 cm	423	42.2	2	66	9	64.3
	≥ 5 cm	580	578	1	33	5	35.7
OS	1 yr	803 (1,744)	46	1 (2)	50	9 (10)	90
	2 yr	275 (1,250)	22	0 (1)	0	6 (7)	86
	3 yr	234 (1,693)	13.8	0 (1)	0	6 (7)	86
	5 yr	144 (1,853)	7.7	0 (1)	0	6 (7)	86

Table 3. *Main features and differences concerning neuroendocrine subtypes. OS: Overall survival; GEJ: Gastroesophageal junction; SCEC: Small cell esophageal cancer; LCEC: Large cell esophageal cancer.*

DISCUSSION

Neuroendocrine esophageal neoplasms are exceedingly rare, and hence there are few large sample clinical studies approaching this issue. Consequently, most of the knowledge is based on neuroendocrine lung neoplasms.

Neuroendocrine lung tumors are classified as low grade (carcinoids) or as high grade (SCEC and LCEC). [120]

SCEC have nuclear appearance, with finely granular chromatin; lack of predominant nucleoli; nuclear fragility; fusiform cells; scant cytoplasm and indistinct cells borders; high mitotic rate; and large area of necrosis. [120] See figure 3.

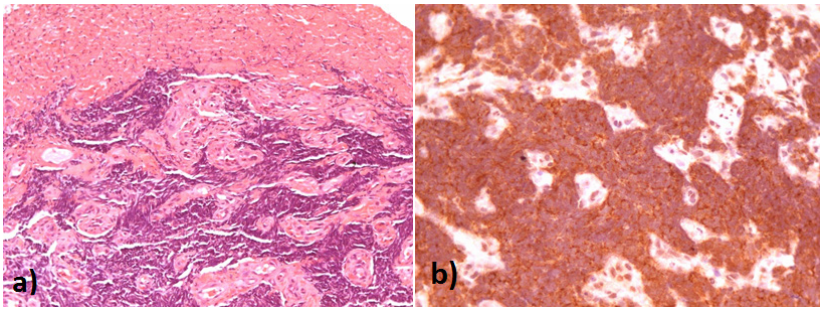

Figure 3. *Small cell esophageal carcinoma (SCEC). High power view of infiltrative proliferation of round small cells with scanty cytoplasm and dark nuclei with intense crush artifacts lined by ulcerative epithelium (a) (HE, 200x). CD56 positive (b) (400x).*

LCEC presents non-small cell nuclear features (vesicular clumpy chromatin, predominant nucleoli), abundant cytoplasm, and large cell size. [120] See figure 4.

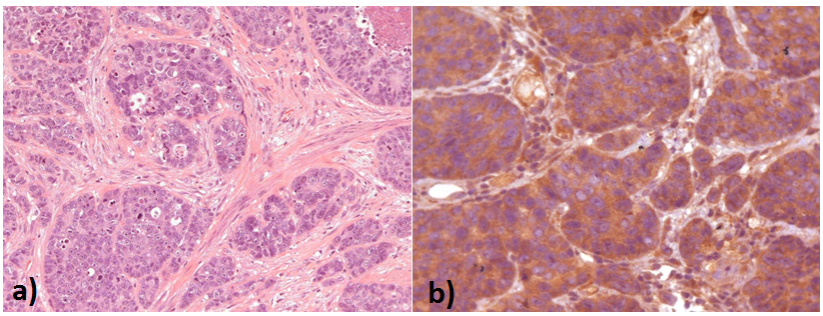

Figure 4. *Large cell esophageal carcinoma (LCEC). Solid nests of large and intermediate cells, with eosinophilic cytoplasm, vesicular nuclei and prominent nucleoli, focal necrosis and high mitotic rate (a) (HE, 200x). Chromogranin positive (400x) (b).*

Carcinoids typical morphology includes coarsely granular “salt and pepper” chromatin, overall uniformity, prominent vascularity, lack of prominent nucleoli, low mitosis rate. Usually no necrosis is seen.[120]

Esophageal high grade tumors tend to be aggressive. Usually, patients are diagnosed lately, with widespread disease, and with poor prognosis. Currently, clinical treatment strategies of high grade cancers neuroendocrine neoplasms are very limited and full of contradiction. High grade neoplasms are often regarded as a systemic disease and, just like in lung cancer, chemotherapy is the mainstay of therapy.[17] Additional therapy (surgery or radiotherapy) should be considered, but randomized controlled trials still unavailable. [80, 116]

Our data suggests a much good prognosis for low grade neuroendocrine tumors, with high overall survival rate. For limited disease (LD) carcinoid, surgical intervention is the treatment of choice. [18]

Although low incidence of esophageal neuroendocrine tumors, our results give a better picture of the behavior of this rare condition. The present study shows this disease affects mainly men in sixties or seventies. Middle and lower esophageal thirds are most frequently affected. Nevertheless, future multicenter efforts are needed for randomized clinical trials evaluating therapeutic guidelines.

REFERENCES

1. Adachi K, Tateno Y, Okada H. An esophageal collision tumor. Clin Gastroenterol Hepatol. 2014 Mar;12(3): 17-8.

2. Akagi I, Miyashita M, Makino H, Nomura T, Shimanuki K, Satake S, Hagiwara N, Uchida E. Small cell carcinoma of the esophagus: a case report. J Nippon Med Sch. 2014;81(2):97-100.

3. Ando T, Hosokawa A, Yamawaki H, Hasumoto Y, Kajiura S, Itaya Y, Ueda A,Suzuki N, Nishikawa J, Fujinami H, Miyazaki T, Ogawa K, Sugiyama T. Esophageal small-cell carcinoma with syndrome of inappropriate secretion of antidiuretic hormone. Intern Med. 2011;50(10):1099-103.

4. Atsumi K, Shioyama Y, Nomoto S, Ohga S, Toba T, Sasaki T, Kunitake N, Yoshitake T, Nakamura K, Honda H. Chemoradiation for small cell esophageal carcinoma: report of 11 cases from multi-institution experience. J Radiat Res. 2010;51(1):15-20.

5. Asayama M, Fuse N, Yoshino T, Yano T, Tahara M, Doi T, Fujii S, Ohtsu A. Amrubicin for the treatment of neuroendocrine carcinoma of the gastrointestinal tract: a retrospective analysis of five cases. Cancer Chemother Pharmacol. 2011 Nov;68(5):1325-30.

6. Atsumi K, Shioyama Y, Nomoto S, Ohga S, Toba T, Sasaki T, Kunitake N, Yoshitake T, Nakamura K, Honda H. Chemoradiation for small cell esophageal carcinoma: report of 11 cases from multi-institution experience. J Radiat Res. 2010;51(1):15-20.

7. Babich JP, Klein J, Khullar P, Friedel DM. Endoscopic mucosal resection of a mid-esophageal carcinoid with EUS guidance. Endoscopy. 2010;42 Suppl 2:E302-3.

8. Basu S, Nair N. (18)FDG PET in primary oat cell carcinoma of the esophagus. Indian J Cancer. 2005 Jan-Mar;42(1):60-2.

9. Bennouna J, Bardet E, Deguiral P, Douillard JY. Small cell carcinoma of the esophagus: analysis of 10 cases and review of the published data. Am J Clin Oncol. 2000 Oct;23(5):455-9.

10. Bibeau F, Chateau MC, Guiu M, Assenat E, Azria D, Lavaill R, Ychou M, Boissière-Michot F. Small cell carcinoma with concomitant adenocarcinoma arising in a Barrett's oesophagus: report of a case with a favourable behaviour. Virchows Arch. 2008 Jan;452(1):103-7.

11. Briggs JC, Ibrahim NB. Oat cell carcinomas of the oesophagus: a clinico-pathological study of 23 cases. Histopathology. 1983 Mar;7(2):261-77.

12. Brown RS Jr, Peppercorn MA, Farraye FA, Glotzer DJ, Antonioli DA, Taylor G. Carcinoid tumor of the esophagus. J Clin Gastroenterol. 1994 Dec;19(4):338-9.

13. Caldwell CB, Bains MS, Burt M. Unusual malignant neoplasms of the esophagus. Oat cell carcinoma, melanoma, and sarcoma. J Thorac Cardiovasc Surg. 1991 Jan;101(1):100-7.

14. Cary NR, Barron DJ, McGoldrick JP, Wells FC. Combined oesophageal adenocarcinoma and carcinoid in Barrett's oesophagitis: potential role of enterochromaffin-like cells in oesophageal malignancy. Thorax. 1993 Apr;48(4):404-5.

15. Casas F, Ferrer F, Farrús B, Casals J, Biete A. Primary small cell carcinoma of the esophagus: a review of the literature with emphasis on therapy and prognosis. Cancer. 1997 Oct 15;80(8):1366-72.

16. Chatni SS, Ravindran HK, Narayanan A, Balakrishnan V. Small cell carcinoma of the esophagus. Saudi J Gastroenterol. 2008 Jul;14(3):149-50.

17. Chen SB, Yang JS, Yang WP, Weng HR, Li H, Liu DT, Chen YP. Treatment and prognosis of limited disease primary small cell carcinoma of esophagus. Dis Esophagus. 2011 Feb;24(2):114-9.

18. Chen KC, Chang YL, Pan CT, Lee YC. Esophageal atypical carcinoid tumor with tracheal invasion. J Thorac Cardiovasc Surg. 2007 Aug;134(2):524-5.

19. Chen WW, Wang F, Chen S, Wang L, Ren C, Luo HY, Wang FH, Li YH, Zhang DS, Xu RH. Detailed analysis of prognostic factors in primary esophageal small cell carcinoma. Ann Thorac Surg. 2014 Jun;97(6):1975-81.

20. Chin K, Baba S, Hosaka H, Ishiyama A, Mizunuma N, Shinozaki E, Suenaga M, Kozuka T, Seto Y, Yamamoto N, Hatake K. Irinotecan plus cisplatin for therapy of small-cell carcinoma of the esophagus: report of 12 cases from single institution experience. Jpn J Clin Oncol. 2008 Jun;38(6):426-31.

21. Chino O, Makuuchi H, Ozawa S, Shimada H, Nishi T, Kise Y, Hara T, Yamamoto S, Kazuno A, Kajiwara H. Small Cell Type of Esophageal Neuroendocrine Carcinoma Resembling a Submucosal Tumor. Tokai J Exp Clin Med. 2015 Jun 20;40(2):36-9.

22. Chong FK, Graham JH, Madoff IM. Mucin-producing carcinoid ("composite tumor") of upper third of esophagus: a variant of carcinoid tumor. Cancer. 1979 Nov;44(5):1853-9.

23. Chow V, Law S, Lam KY, Luk JM, Wong J. Telomerase activity in small cell esophageal carcinoma. Dis Esophagus. 2001;14(2):139-42.

24. Chuah SK, Hu TH, Kuo CM, Chiu KW, Kuo CH, Wu KL, Chou YP, Lu SN, Chiou SS, Changchien CS, Eng HL. Upper gastrointestinal carcinoid tumors incidentally found by endoscopic examinations. World J Gastroenterol. 2005 Nov 28;11(44):7028-32.

25. Clark T, Lee MJ, Munk PL. Primary small-cell carcinoma of the oesophagus with spontaneous oesophageal perforation following chemotherapy. Australas Radiol. 1996 Aug;40(3):250-3.

26. Cook MG, Eusebi V, Betts CM. Oat-cell carcinoma of the oesophagus: a recently recognized entity. J Clin Pathol. 1976 Dec;29(12):1068-73.

27. Cox PM, Vazir MH, Petty RK, Law S, Dhillon AP. Cerebellar cortical degeneration in association with small-cell carcinoma of the oesophagus. Neuropathol Appl Neurobiol. 1989 Mar-Apr;15(2):175-83.

28. Craig SR, Carey FA, Walker WS, Cameron EW. Primary small-cell cancer of the esophagus. J Thorac Cardiovasc Surg. 1995 Feb;109(2):284-8.

29. Deepak P, Devi R, Pillai H. Esophageal small cell carcinoma with synchronous renal cell carcinoma: a case report with review of the literature. Case Rep Gastroenterol. 2011 Apr 13;5(1):196-200.

30. del Valle Ruiz SR, Torres Bermúdez JR, Montoya Tabares MJ, Merino Montes J, Sánchez de la Villa G. [Extrapulmonary small cell carcinoma located in the oesophagus. Cir Esp. 2010 Jul;88(1):47-8.

31. Doherty MA, McIntyre M, Arnott SJ. Oat cell carcinoma of esophagus: a report of six British patients with a review of the literature. Int J Radiat Oncol Biol Phys. 1984 Jan;10(1):147-52.

32. Eccles DM, Allan SG, Sang CT, Cornbleet MA. Small cell carcinoma of the oesophagus: report of three cases and review of published cases. Thorax. 1989 Sep;44(9):749-50.

33. Einspanier GR, Caleel RT, Milford AF 3rd. Carcinoid tumors of the esophagus: report of a case. J Am Osteopath Assoc. 1987 Jul;87(7):500-3.

34. Enzinger PC, Mayer. R. Esophageal Cancer. N Engl J Med. 2003; 349: 2241-52.

35. Feng JF, Huang Y, Zhao Q, Chen QX. Clinical significance of preoperative neutrophil lymphocyte ratio versus platelet lymphocyte ratio in patients with small cell carcinoma of the esophagus. ScientificWorldJournal. 2013 Sep 5;2013:504365.

36. Feng W, Harada H, Zhang P, Mitsuya K, Zheng X, Yasui H, Nakasu Y, Chen M, Nishimura T. Metastatic brain tumors from small-cell esophageal cancer: clinical characteristics and outcome. J Cancer Res Ther. 2014 Dec;10 Suppl:256-8.

37. Fenlon HM, O'Keane C, Carney DN, Breatnach E. Imaging of small cell carcinoma of the oesophagus. Clin Radiol. 1995 Sep;50(9):634-8.

38. Fukuchi M, Sakurai S, Tsukagoshi R, Naitoh H, Kuwano H. A case of large cell neuroendocrine carcinoma of the esophagogastric junction. Esophagus. 2015;12:295-9.

39. Funakoshi S, Hashiguchi A, Teramoto K, Miyata N, Kurita S, Adachi M, Hamamoto Y, Higuchi H, Takaishi H, Hibi T. Second-line chemotherapy for refractory small cell neuroendocrine carcinoma of the esophagus that relapsed after complete remission with irinotecan plus cisplatin therapy: Case report and review of the literature. Oncol Lett. 2013 Jan;5(1):117-122.

40. Gao R, Zhang Y, Wen XP, Fu J, Zhang GJ. Chemotherapy with cisplatin or carboplatin in combination with etoposide for small-cell esophageal cancer: a systemic analysis of case series. Dis Esophagus. 2014 Nov-Dec;27(8):764-9.

41. Gollard R, Ellis C, VanderHarten C. Small cell/neuroendocrine tumors of the esophagus: presentation of two cases and review of the literature. Tumori. 2010Sep-Oct;96(5):780-3.

42. González LM, Sanz-Esponera J, Saez C, Alvarez T, Sierra E, Sanz-Ortega J.Case report: esophageal collision tumor (oat cell carcinoma and adenocarcinoma) in Barrett's esophagus: immunohistochemical, electron microscopy and LOH analysis. Histol Histopathol. 2003 Jan;18(1):1-5.

43. Goscinski MA, Xu R, Zhou F, Wang J, Yang H, Huang R, Li Y, Larsen SG, Gierckskγ KE, Nesland JM, Suo Z. Nuclear, cytoplasmic, and stromal expression of ZEB1 in squamous and small cell carcinoma of the esophagus. APMIS. 2015 Dec;123(12):1040-7.

44. Goto T, Watabe H, Kawakami T, Watanabe M, Nakano K, Takai A, Kitazawa E, Sato S, Tajima Y, Mizuguchi K, Kikuchi K, Miyakawa H, Murakawa Y. [A case of small cell carcinoma of the esophagus with remarkable response to chemotherapy with CPT-11 and CDDP]. Nihon Shokakibyo Gakkai Zasshi. 2007 Aug;104(8):1204-11.

45. Gumprich T, Johnen G, Hummel T, Jaworska M, Schmitz I, Müller KM. [A rare case of a neuroendocrine carcinoma of the esophagus. Intermediate between a wel-differentiated neuroendocrine carcinoma and a low-differentiated neuroendocrine carcinoma]. Pathologe. 2004 May;25(3):229-34.

46. Gupta NM, Goenka MK, Atri A, Vaiphei K. Carcinoid tumour of the oesophagus: a rare oesophageal cancer. Eur J Surg. 1996 Oct;162(10):841-4.

47. Heyes FL, Ayres J, Matthews HR. Oat cell carcinoma of esophagus. Int J Radiat Oncol Biol Phys. 1985 Aug;11(8):1573.

48. Hoang MP, Hobbs CM, Sobin LH, Albores-Saavedra J. Carcinoid tumor of the esophagus: a clinicopathologic study of four cases. Am J Surg Pathol. 2002 Apr;26(4):517-22.

49. Horai T, Kobayshi A, Tateishi R, Wada A, Taniguchi H, Taniguchi K, Sano M, Tamura H. A cytologic

study on small cell carcinoma of the esophagus. Cancer. 1978 May;41(5):1890-6.

50. Hosseini S, Salek R, Nasrolahi H, Mohammadianpanah M, Judi M. Small Cell Carcinoma of the Esophagus: Clinicopathological Features and Outcome of 22 Cases.Iran Red Crescent Med J. 2015 Nov 1;17(11):e20353.

51. Hou X, Wei JC, Wu JX, Wang X, Fu JH, Lin P, Yang HX. Multidisciplinary modalities achieve encouraging long-term survival in resectable limited-disease esophageal small cell carcinoma. PLoS One. 2013 Jul 9;8(7):e69259.

52. Hsu PK, Li AF, Hsu WH. Simultaneous thoracotomy and laparotomy for small cell carcinoma of oesophagogastric junction. ANZ J Surg. 2008 Aug;78(8):723-4.

53. Huang Q, Wu H, Nie L, Shi J, Lebenthal A, Chen J, Sun Q, Yang J, Huang L, Ye Q. Primary high-grade neuroendocrine carcinoma of the esophagus: a clinicopathologic and immunohistochemical study of 42 resection cases. Am J Surg Pathol. 2013 Apr;37(4):467-83.

54. Huang YL, Chou SH, Chai CY, Hsu JS. Small cell neuroendocrine carcinoma of the esophagus. Kaohsiung J Med Sci. 2015 Feb;31(2):108-9.

55. Hudson E, Powell J, Mukherjee S, Crosby TD, Brewster AE, Maughan TS, Bailey H, Lester JF. Small cell oesophageal carcinoma: an institutional experience and review of the literature. Br J Cancer. 2007 Mar 12;96(5):708-11.

56. Huncharek M, Muscat J. Small cell carcinoma of the esophagus. The Massachusetts General Hospital experience, 1978 to 1993. Chest. 1995 Jan;107(1):179-81.

57. Imai T, Sannohe Y, Okano H. Oat cell carcinoma (apudoma) of the esophagus: a case report. Cancer. 1978 Jan;41(1):358-64.

58. Isoyama Y, Shioyama Y, Nomoto S, Ohga S, Nonoshita T, Onishi K, Matsuura S, Atsumi K, Terashima K, Hirata H, Honda H. Carboplatin and etoposide combined with radiotherapy for limited-stage small-cell esophageal carcinoma: three cases and review of the literature. Jpn J Radiol. 2010 Apr;28(3):181-7.

59. Lv J, Linag J, Wang J, Wang L, He J, Xiao Z, Yin W. Primary Small Cell Carcinoma of the Esophagus. J Thorac Oncol. 2008;3: 1460–1465.

60. Johnson FE, Clawson MC, Bashiti HM, Silverberg AB, Broun GO Jr. Small cell undifferentiated carcinoma of the esophagus. Case report with hormonal studies. Cancer. 1984 Apr 15;53(8):1746-51.

61. Kadhim MM, Jespersen ML, Pilegaard HK, Nordsmark M, Villadsen GE. Mixed Adenoneuroendocrine Carcinoma Is a Rare but Important Tumour Found in the Oesophagus. Case Rep Gastrointest Med. 2016;2016:9542687.

62. Kanamoto A, Nakanishi Y, Ochiai A, Shimoda T, Yamaguchi H, Tachimori Y, Kato H, Watanabe H. A case of small polypoid esophageal carcinoma with multidirectional differentiation, including neuroendocrine, squamous, ciliated glandular, and sarcomatous components. Arch Pathol Lab Med. 2000 Nov;124(11):1685-7.

63. Kanno K, Hikichi T, Saito K, Watanabe K, Takagi T, Shibukawa G, Wakatsuki T, Imamura H, Takahashi Y, Sato A, Sato M, Irisawa A, Obara K, Ohira H. A case of esophageal small cell carcinoma associated with hypercalcemia causing severe acute pancreatitis. Fukushima J Med Sci. 2007 Jun;53(1):51-60.

64. Kitajima T, Kaida S, Lee S, Haruta S, Shinohara H, Ueno M, Suyama K, Oota Y, Fujii T, Udagawa H. Mixed adeno(neuro)endocrine carcinoma arising from the ectopic gastric mucosa of the upper

thoracic esophagus. World J Surg Oncol. 2013 Sep 4;11:218. doi: 10.1186/1477-7819-11-218.

65. Koide N, Saito H, Suzuki A, Sato T, Koiwai K, Nakamura N, Miyagawa S. Clinicopathologic features and histochemical analyses of proliferative activity and angiogenesis in small cell carcinoma of the esophagus. J Gastroenterol. 2007 Dec;42(12):932-8.

66. Krishnatreya M, Kataki AC, Sharma JD, Borthakur BB, Kalita M. Epidemiology of primary small cell carcinoma of the esophagus: A retrospective study. South Asian J Cancer. 2014 Oct;3(4):231-2.

67. Ku GY, Minsky BD, Rusch VW, Bains M, Kelsen DP, Ilson DH. Small-cell carcinoma of the esophagus and gastroesophageal junction: review of the Memorial Sloan-Kettering experience. Ann Oncol. 2008 Mar;19(3):533-7.

68. Kukar M, Groman A, Malhotra U, Warren GW, Bogner P, Nwogu CE, Demmy TL, Yendamuri S. Small cell carcinoma of the esophagus: a SEER database analysis. Ann Surg Oncol. 2013 Dec;20(13):4239-44.

69. Kuo CH, Hsieh CC, Chan ML, Li AF, Huang MH, Hsu WH, Hsu HS. Small cell carcinoma of the esophagus: a report of 16 cases from a single institution and literature review. Ann Thorac Surg. 2011 Feb;91(2):373-8.

70. Kuriry H, Swied AM. Large-Cell Neuroendocrine Carcinoma of the Esophagus: A Case from Saudi Arabia. Case Rep Gastroenterol. 2015 Oct 21;9(3):327-34.

71. Lam KY, Law S, Tung PH, Wong J. Esophageal small cell carcinomas: clinicopathologic parameters, p53 overexpression, proliferation marker, and their impact on pathogenesis. Arch Pathol Lab Med. 2000 Feb;124(2):228-33.

72. Law SY, Fok M, Lam KY, Loke SL, Ma LT, Wong J. Small cell carcinoma of the esophagus. Cancer. 1994 Jun 15;73(12):2894-9.

73. Lee YT, Chiu PW, Choi PC, Sung JJ. Esophageal small-cell cancer mimicking stromal tumor. Endoscopy. 2006;38 Suppl 2:E21-2.

74. Lee CG, Lim YJ, Park SJ, Jang BI, Choi SR, Kim JK, Kim YT, Cho JY, Yang CH, Chun HJ, Song SY; Neuroendocrine tumor study group. The clinical features and treatment modality of esophageal neuroendocrine tumors: a multicenter study in Korea. BMC Cancer. 2014 Aug 7;14:569.

75. Li J, Chen X, Shen Y, Hou Y, Zhang S, Wang H, Feng M, Tan L, Wang Q, Zeng Z. A rare collision tumor of squamous carcinoma and small cell carcinoma in esophagus involved with separate lymph nodes: a case report. J Thorac Dis. 2013 Oct;5(5):E203-6.

76. Lichtenstein S, Albert NE, Muchnik A, Abraham M. Small cell carcinoma: an unusual location in a young healthy female. J Gastrointestin Liver Dis. 2011 Dec;20(4):427-30.

77. Lim CS, Park SJ, Park MI, Moon W, Kim HH, Lee JS, Kim BJ, Ku DY. Successful endoscopic mucosal resection of a low esophageal carcinoid tumor. Clin Endosc. 2013 Sep;46(5):576-8.

78. Lü JM, Liang J, Wang JW, He J, Xiao ZF, Zhang HX, Chen DF, Feng QF, Wang LH. [Clinical analysis of 126 patients with primary small cell carcinoma of the esophagus]. Zhonghua Zhong Liu Za Zhi. 2009 Feb;31(2):121-5.

79. Lu J, Xue LY, Lu N, Zou SM, Liu XY, Wen P. Superficial primary small cell carcinoma of the esophagus: clinicophatological and immunohistocemical analysis of 15 cases. Dis Esophagus. 2010;23:153-9

80. Lu XJ, Luo JD, Ling Y, Kong YZ, Feng LL, Zhou J, Wang F. Management of Small Cell Carcinoma of Esophagus in China. J Gastrointest Surg. 2013. 17:1181–87

81. Macaigne G, Boivin JF, Chayette C, Chaieb S, Deplus R. [Small-cell carcinoma of the esophagus: presentation of a case and review of the literature]. Gastroenterol Clin Biol. 1999 Aug-Sep;23(8-9):988-90.

82. Madroszyk A, Egreteau J, Martin L, Queneau PE, Bosset JF, Merrouche Y. Small-cell carcinoma of the esophagus: report of three cases and review of the literature with emphasis on therapy. Ann Oncol. 2001 Sep;12(9):1321-5.

83. Maheswari GK, Baboo HA, Patel MH, Gopal U, Wadhwa MK. Primary malignant carcinoid tumor of the esophagus. Turk J Cancer. 2000;30(1):40-3

84. Makino H, Tajiri T, Onda M, Sasajima K, Miyashita M, Nomura T, Maruyama H, Nagasawa S, Tsuchiya Y, Hagiwara N, Yamashita K, Takubo K. Effectiveness of preoperative chemotherapy using carboplatin (CBDCA) and surgery against an esophageal mall cell carcinoma. Dis Esophagus. 2002;15(3):237-41.

85. Martin R, Natesha RK, Hsu HK, Thompson I, Hoover EL. Synchronous small cell and squ amous cell carcinoma of the esophagus: case report and review of embryogenesis. J Tenn Med Assoc. 1988 May;81(5):288-90.

86. Maru DM, Khurana H, Rashid A, Correa AM, Anandasabapathy S, Krishnan S, Komaki R, Ajani JA, Swisher SG, Hofstetter WL. Retrospective study of clinicopathologic features and prognosis of high-grade neuroendocrine carcinoma of the esophagus. Am J Surg Pathol. 2008 Sep;32(9):1404-11.

87. Fattahi Masoum SH, Sharifi N, Taraz Jamshidi S, Sharifian A, Rezaee R. Primary Small Cell Carcinoma of the Esophagus (PSCEC) Associated with Paraneoplastic Sweating Syndrome: A Case Report and Literature Review. Iran J Otorhinolaryngol. 2015 Nov;27(83):463-7.

88. Matsuda K, Sakurada K, Kokubo Y, Sato S, Nakazato Y, Kayama T. Esophageal neuroendocrine tumor metastatic to the pineal region. Brain Tumor Pathol. 2014 Jul;31(3):192-7.

89. Matsunaga M, Miwa K, Noguchi T, Sasaki Y. Small cell carcinoma of gastro-oesophageal junction with remarkable response to chemo-radiotherapy. BMJ Case Rep. 2012 Jul 25;2012.

90. Matsuoka M, Boku N, Yoshino T, Hironaka S, Onozawa Y, Fukutomi A, Zenda S, Yamazaki K, Yasui H, Hasuike N, Inui T, Yamaguchi Y, Ono H, Kamata M. Small cell carcinoma of the esophagus responding to fourth-line chemotherapy with weekly paclitaxel. Int J Clin Oncol. 2005 Dec;10(6):429-32.

91. Matsusaka T, Watanabe H, Enjoji M. Anaplastic carcinoma of the esophagus. Report of three cases and their histogenetic consideration. Cancer. 1976 Mar;37(3):1352-8.

92. McCullen M, Vyas SK, Winwood PJ, Loehry CA, Parham DM, Hamblin T. Long-term survival associated with metastatic small cell carcinoma of the esophagus treated by chemotherapy, autologous bone marrow transplantation, and adjuvant radiation therapy. Cancer. 1994 Jan 1;73(1):1-4.

93. Medgyesy CD, Wolff RA, Putnam JB Jr, Ajani JA. Small cell carcinoma of the esophagus: the University of Texas M. D. Anderson Cancer Center experience and literature review. Cancer. 2000 Jan 15;88(2):262-7.

94. Mimori K, Mori M, Kuwano H, Sugimachi K. Hyperthermochemoradiotherapy is effective for small cell carcinoma of the esophagus. J Surg Oncol. 1995 May;59(1):63-6.

95. Mitani M, Kuwabara Y, Shinoda N, Sato A, Fujii Y. Long-term survivors after the resection of limited esophageal small cell carcinoma. Dis Esophagus. 2000;13(3):259-61.

96. Mori M, Matsukuma A, Adachi Y, Miyagahara T, Matsuda H, Kuwano H, Sugimachi K, Enjoji M. Small cell carcinoma of the esophagus. Cancer. 1989 Feb 1;63(3):564-73.

97. Muguruma K, Ohira M, Tanaka H, Kubo N, Yamashita Y, Sawada T, Wakasa K, Hirakawa K. Long-term survival of advanced small cell carcinoma of the esophagus after resection: a case report. Anticancer Res. 2013 Feb;33(2):595-600.

98. Mulder LD, Gardiner GA, Weeks DA. Primary small cell carcinoma of the esophagus: case presentation and review of the literature. Gastrointest Radiol. 1991 Winter;16(1):5-10.

99. Nakajima Y, Zenda S, Minashi K, Yano T, Tahara M, Doi T, Onozawa M, Nihei K, Fujii S, Ohtsu A. Non-surgical approach to small cell carcinoma of the esophagus: does this rare disease have the same tumor behavior as SCLC? Int J Clin Oncol.2012 Dec;17(6):610-5.

100. Nawroz IM. Malignant carcinoid tumour of oesophagus. Histopathology. 1987 Aug;11(8):879-80.

101. Nayal B, Vasudevan G, Rao AC, Kudva R, Valliathan M, Mathew M, Rao L. Primary Small Cell Carcinoma of The Esophagus - An Eight Year Retrospective Study. J Clin Diagn Res. 2015 May;9(5):EC04-6.

102. Nemoto K, Zhao HJ, Goto T, Ogawa Y, Takai Y, Matsushita H, Takeda K, Takahashi C, Saito H, Yamada S. Radiation therapy for limited-stage small-cell esophageal cancer. Am J Clin Oncol. 2002 Aug;25(4):404-7.

103. Nevarez A, Saftoiu A, Bhutani MS. Primary small cell carcinoma of esophagus: clinic-pathological features and therapeutic options. Current Health Sciences Journal. 2011;37(1):31-4

104. Nichols GL, Kelsen DP. Small cell carcinoma of the esophagus. The Memorial Hospital experience 1970 to 1987. Cancer. 1989 Oct 1;64(7):1531-3.

105. Tokunaga N, Itaba S, Nakamura K, Yamada M, Okamoto R, Aso A, Igarashi H, Akiho H, Ito T, Takayanagi R, Goto A. [A case of lymph node metastasis from esophageal small-cell-type endocrine cell carcinoma diagnosed by endoscopic ultrasound-guided fine-needle aspiration]. Nihon Shokakibyo Gakkai Zasshi. 2012 Aug;109(8):1360-6.

106. Nishimaki T, Suzuki T, Fukuda T, Aizawa K, Tanaka O, Muto T. Primary small cell carcinoma of the esophagus with ectopic gastrin production. Report of a case and review of the literature. Dig Dis Sci. 1993 Apr;38(4):767-71.

107. Noguchi T, Takeno S, Kato T, Wada S, Noguchi T, Uchida Y, Kashima K, Yokoyama S. Small cell carcinoma of the esophagus; clinicopathological and immunohistochemical analysis of six cases. Dis Esophagus. 2003;16(3):252-8.

108. Ohmura Y, Takiyama W, Mandai K, Doi T, Nishikawa Y. Small cell carcinoma of the esophagus: a case report. Jpn J Clin Oncol. 1997 Apr;27(2):95-100.

109. Okuma HS, Iwasa S, Shoji H, Takashima A, Okita N, Honma Y, Kato K, Hamaguchi T, Yamada Y, Shimada Y. Irinotecan plus cisplatin in patients with extensive-disease poorly differentiated neuroendocrine carcinoma of the esophagus. Anticancer Res. 2014 Sep;34(9):5037-41.

110. Okumura T, Shimada Y, Omura T, Hirano K, Nagata T, Tsukada K. MicroRNA profiles to predict postoperative prognosis in patients with small cell carcinoma of the esophagus. Anticancer Res. 2015 Feb;35(2):719-27.

111. Liñán Padilla A, Milla Sabas A, Abad Zamora JM, Vázquez Medina A, Ibáñez F, Alcántara F, Hernández de la Torre JM. [Oat-cell carcinoma of the esophagus presentation of two cases and literature review]. Rev Esp Enferm Dig. 2007 Jul;99(7):415-9.

112. Pantvaidya GH, Pramesh CS, Deshpande MS, Jambhekar NA, Sharma S, Deshpande RK. Small cell carcinoma of the esophagus: the Tata Memorial Hospital experience. Ann Thorac Surg. 2002 Dec;74(6):1924-7.

113. Partensky C, Chayvialle JA, Berger F, Souquet JC, Moulinier B. Five-year survival after transhiatal resection of esophageal carcinoid tumor with a lymph node metastasis. Cancer. 1993 Oct 15;72(8):2320-2.

114. Poynton AR, Walsh TN, Kelly A, Harney M, Stuart R, Daly PA, Hennessy TP. Small cell carcinoma of the oesophagus. Eur J Surg Oncol. 1997 Dec;23(6):509-12.

115. Purdy S, Gaffney EF. Ultrastructural and immunocytochemical definition of component neoplasms in an unusual gastro-oesophageal collision tumour. Histopathology. 1986 May;10(5):525-34.

116. Raja S, Rice TW, Rajeswaran J, Zhong J, Blackstone EH. Esophageal Small-Cell Cancer: Study of a Rare Disease. Dis Esophagus. 2013. 26: 690-5.

117. Rankin R, Nirodi NS, Browne MK. Carcinoid tumour of the oesophagus: report of a case. Scott Med J. 1980 Jul;25(3):245-9.

118. Ready AR, Soul JO, Newman J, Matthews HR. Malignant carcinoid tumour of the oesophagus. Thorax. 1989 Jul;44(7):594-6.

119. Reid HA, Richardson WW, Corrin B. Oat cell carcinoma of the esophagus. Cancer. 1980 May 1;45(9):2342-7.

120. Rekhtman N. Neuroendocrine Tumors of the Lung. An Update. Arch Pathol Lab Med. 2010. 134: 1628-38.

121. Reyes CV, Chejfec G, Jao W, Gould VE. Neuroendocrine carcinomas of the esophagus. Ultrastruct Pathol. 1980 Jul-Sep;1(3):367-76.

122. Rice TW, Blackstone EH, Rusch VW. 7th Edition of AJCC Cancer Staging Manual: Esophagus and Esophagogastric Junction. Ann Surg Oncol. 2010. 17: 1721-4.

123. Rosenthal SN, Lemkin JA. Multiple small cell carcinomas of the esophagus. Cancer. 1983 May 15;51(10):1944-6.

124. Sabanathan S, Graham GP, Salama FD. Primary oat cell carcinoma of the oesophagus. Thorax. 1986 Apr;41(4):318-21.

125. Sahai P, Baghmar S, Nath D, Arora S, Bhasker S, Gogia A, Sikka K, Kumar R, Chander S. Extrapulmonary Small Cell Carcinoma - a Case Series of Oropharyngea and Esophageal Primary Sites Treated with Chemo-Radiotherapy. Asian Pac J Cancer Prev. 2015;16(16):7025-9.

126. Sahnane N, Furlan D, Monti M, Romualdi C, Vanoli A, Vicari E, Solcia E, Capella C, Sessa F, La Rosa S. Microsatellite unstable gastrointestinal neuroendocrine carcinomas: a new clinicopathologic entity. Endocr Relat Cancer. 2015 Feb;22(1):35-45.

127. Sato T, Mukai M, Ando N, Tashiro Y, Iri H, Abe O, Watanabe Y. Small cell carcinoma (non-oat cell type) of the esophagus concomitant with invasive squamous cell carcinoma and carcinoma in situ. A case report. Cancer. 1986 Jan 15;57(2):328-32.

128. Saw EC, Yu GS, Wagner G, Heng Y. Synchronous primary neuroendocrine carcinoma and adenocarcinoma in Barrett's esophagus. J Clin Gastroenterol. 1997 Mar;24(2):116-9.

129. Schuerle T, Aoun E, Farah K. Small cell carcinoma of the oesophagus: a rare cause of dysphagia. BMJ Case Rep. 2013 Sep 3;2013. pii: bcr2013200468.

130. Shimoda T, Koizumi W, Tanabe S, Higuchi K, Sasaki T, Nakayama N, Azuma M, Saigenji K, Katou T, Ogino M. Small-cell carcinoma of the esophagus associated with a paraneoplastic neurological syndrome: a case report documenting a complete response. Jpn J Clin Oncol. 2006 Feb;36(2):109-12.

131. Shinohara Y, Takeno S, Takahashi Y, Moroga T, Yamashita S, Kawahara K. Successful chemoradiotherapy for small-cell carcinoma of the esophagus in an octogenarian Japanese woman: report of the oldest case and review of long-term survival cases. Ann Thorac Cardiovasc Surg. 2014;20(3):237-42.

132. Shirafuji T, Kanda F, Sekiguchi K, Higuchi M, Yokozaki H, Tanaka K, Takahashi H, Toda T. Anti-Hu-associated paraneoplastic encephalomyelitis with esophageal small cell carcinoma. Intern Med. 2012;51(17):2423-7.

133. Siegal A, Swartz A, Aronheim M. Malignant carcinoid tumour of the oesophagus. Thorax. 1991 Jan;46(1):76.

134. Song Y, Wang W, Tao G, Zhu W, Zhou X, Pan P. Survival benefit of radiotherapy to patients with small cell esophagus carcinoma - An analysis of Surveillance Epidemiology and End Results (SEER) data. Oncotarget. 2015 Dec 26. doi:10.18632/oncotarget.6764.

135. Sun KL, He J, Cheng GY, Chai LX. Management of primary small cell carcinoma of the esophagus. Chin Med J (Engl). 2007 Mar 5;120(5):355-8.

136. Tanabe G, Kajisa T, Shimazu H, Yoshida A. Effective chemotherapy for small cell carcinoma of the esophagus. Cancer. 1987 Dec 1;60(11):2613-6.

137. Tanaka T, Matono S, Nagano T, Nishimura K, Murata K, Yamana H, Shirouzu K,Fujita H. Surgical management for small cell carcinoma of the esophagus. Dis Esophagus. 2010 Aug;23(6):502-5.

138. Terada T. Small cell neuroendocrine carcinoma of the esophagus: report of 6 cases with immunohistochemical and molecular genetic analysis of KIT and PDGFRA. Int J Clin Exp Pathol. 2013;6(3):485-91.

139. Tetreault SA, Kossman C, Mason J. Syngeneic bone marrow transplantation for small cell carcinoma of the esophagus. Bone Marrow Transplant. 1999 Oct;24(7):813-4.

140. Travis, WD, Brambilla, E, Muller-Hermelink, HK, Harris, CC. The concept of pulmonary neuroendocrine tumours. In: Pathology & Genetics: Tumours of the Lung, Pleura, Thymus, and Heart. IARC Press, Lyon 2004; p.19.

141. Veits L, Lang-Schwarz C, Volkholz H, Falkeis C, Vieth M, Schulz H. Mixed adenoneuroendocrine carcinoma (MANEC) of the esophagogastric junction predominantly consisting of poorly differentiated neuroendocrine carcinoma. Endoscopy. 2013;45 Suppl 2 UCTN:E16-7.

142. Vera-Mémdez FJ, Barón JM, Hallal H, García-Solano J, Martínez-Albadalejo M. [Primary undifferentiated small cell carcinoma of the esophagus: case report and literature review]. Gastroenterol Hepatol. 2001 Oct;24(8):410-1.

143. Vos B, Rozema T, Miller RC, Hendlisz A, Van Laethem JL, Khanfir K, Weber DC, El Nakadi I, Van Houtte P. Small cell carcinoma of the esophagus: a multicenter Rare Cancer Network study. Dis

Esophagus. 2011 May;24(4):258-64.

144. Wakahama O, Nishikawa S, Miyashita K, Kudou T, Nagasaka A, Higuchi A. Carcinoid tumor of the esophagus: report of a case. Gastroenterol Endosc. 2000;42(6):1058-62

145. Walker SJ, Steel A, Cullen MH, Matthews HR. Treatment of oesophageal small cell carcinoma by combined chemotherapy and surgical resection: report of two cases and review of published cases. Thorax. 1989 Sep;44(9):751-2.

146. Wilson CI, Summerall J, Willis I, Lubin J, Inchausti BC. Esophageal collision tumor (Large cell neuroendocrine carcinoma and papillary carcinoma) arising in a Barrett esophagus. Arch Pathol Lab Med. 2000 Mar;124(3):411-5.

147. Wu Z, Ma JY, Yang JJ, Zhao YF, Zhang SF. Primary small cell carcinoma of esophagus: report of 9 cases and review of literature. World J Gastroenterol. 2004 Dec 15;10(24):3680-2.

148. Xie MR, Xu SB, Sun XH, Ke L, Mei XY, Liu CQ, Ma DC. Role of surgery in the management and prognosis of limited-stage small cell carcinoma of the esophagus. Dis Esophagus. 2015 Jul;28(5):476-82.

149. Yachida S, Matsushita K, Usuki H, Wanibuchi H, Maeba T, Maeta H. Long-term survival after resection for small cell carcinoma of the esophagus. Ann Thorac Surg. 2001 Aug;72(2):596-7.

150. Yagi M, Abe Y, Sasaki Y, Nomura E, Sato T, Iwano D, Yoshizawa K, Sakuta K, Kanno N, Nishise S, Ueno Y. Esophageal carcinoid tumor treated by endoscopic resection. Dig Endosc. 2015 May;27(4):527-30.

151. Yamamoto J, Ohshima K, Ikeda S, Iwashita A, Kikuchi M. Primary esophageal small cell carcinoma with concomitant invasive squamous cell carcinoma or carcinoma in situ. Hum Pathol. 2003 Nov;34(11):1108-15.

152. Yamamoto S, Tsuda H, Sakano T, Aikoh S, Tamai S, Matsubara O. Esophageal pleomorphic giant cell carcinoma combined with small cell carcinoma. Pathol Int. 2007 Aug;57(8):523-8.

153. Yan H, Wang R, Jiang S, Zhu K, Feng R, Xu X, Meng X. NSE can predict the sensitivity to definitive chemoradiotherapy of small cell carcinoma of esophagus. Med Oncol. 2014 Jan;31(1):796.

154. Yang L, Sun X, Zou Y, Meng X. Small cell type neuroendocrine carcinoma colliding with squamous cell carcinoma at esophagus. Int J Clin Exp Pathol. 2014 Mar 15;7(4):1792-5.

155. Yau KK, Siu WT, Wong DC, Chau CH, Li AC, Law BK, Li MK. Non-operative management of small cell carcinoma of esophagus. Dis Esophagus. 2007;20(6):487-90.

156. Yazıcı O, Ozdemir NY, Sendur MA, Aksoy S, Zengin N. Current approaches for prophylactic cranial irradiation in extrapulmonary small cell carcinoma. Curr Med Res Opin. 2014 Jul;30(7):1327-36.

157. Yekeler E, Koca T, Vural S. A rare cause of the cough: primary small cell carcinoma of esophagus-case report. Case Rep Med. 2012;2012:870783.

158. Yun JP, Zhang MF, Hou JH, Tian QH, Fu J, Liang XM, Wu QL, Rong TH. Primary small cell carcinoma of the esophagus: clinicopathological and immunohistochemical features of 21 cases. BMC Cancer. 2007 Mar 3;7:38.

159. Zhan XK, Sun YK, Zhang W, Wang JW. [Clinical analysis of 81 cases with primary small cell carcinoma of the esophagus]. Zhonghua Zhong Liu Za Zhi. 2008 Dec;30(12):926-9.

160. Zhang Z, Xiao H, Xie F, Zhang H, Chen C, Xiao H, Yang Z, Wang D, Li Z, Wang G. High-incidence of PTEN mutations in Chinese patients with primary small cell carcinoma of the esophagus. BMC Cancer. 2014 Jan 14;14:19.

161. Zhou Q, Zou BW, Xu Y, Xue JX, Meng MB, Liu FJ, Deng L, Ma DY, Ao R, Lu Y. DNA repair gene polymorphisms and clinical outcome of patients with primary small cell carcinoma of the esophagus. Tumour Biol. 2015 Mar;36(3):1539-48.

162. Zhu Y, Qiu B, Liu H, Li Q, Xiao W, Hu Y, Liu M. Primary small cell carcinoma of the esophagus: review of 64 cases from a single institution. Dis Esophagus. 2014 Feb-Mar;27(2):152-8.

SOBRE OS ORGANIZADORES

Nayara Araújo Cardoso: Graduada com titulação de Bacharel em Farmácia com formação generalista pelo Instituto Superior de Teologia Aplicada – INTA. Especialista em Farmácia Clínica e Cuidados Farmacêuticos pela Escola Superior da Amazônia – ESAMAZ. Mestre em Biotecnologia pela Universidade Federal do Ceará – *Campus* Sobral. Membro do Laboratório de Fisiologia e Neurociência, da Universidade Federal do Ceará – *Campus* Sobral, no qual desenvolve pesquisas na área de neurofarmacologia, com ênfase em modelos animais de depressão, ansiedade e convulsão. Atualmente é Farmacêutica Assistente Técnica na empresa Farmácia São João, Sobral – Ceará e Farmacêutica Supervisora no Hospital Regional Norte, Sobral – Ceará.

Renan Rhonalty Rocha: Graduado com titulação de Bacharel em Farmácia com formação generalista pelo Instituto Superior de Teologia Aplicada - INTA. Especialista em Gestão da Assistência Farmacêutica e Gestão de Farmácia Hospitalar pela Universidade Cândido Mendes. Especialista em Análises Clínicas e Toxicológicas pela Faculdade Farias Brito. Especialista em Farmácia Clínica e Cuidados Farmacêuticos pela Escola Superior da Amazônia - ESAMAZ. Especialista em Micropolítica da Gestão e Trabalho em Saúde do Sistema Único de Saúde pela Universidade Federal Fluminense. Farmacêutico da Farmácia Satélite da Emergência da Santa Casa de Sobral, possuindo experiência também em Farmácia Satélite do Centro Cirúrgico. Membro integrante da Comissão de Farmacovigilância da Santa Casa de Misericórdia de Sobral. Farmacêutico proprietário da Farmácia Unifarma em Morrinhos. Foi coordenador da assistência farmacêutica de Morrinhos por dois anos. Mestrando em Biotecnologia pela Universidade Federal do Ceará.

Maria Vitória Laurindo: Graduada com titulação de Bacharel em Enfermagem pelo Centro Universitário INTA – UNINTA. Foi bolsista no hospital da Santa Casa de Misericórdia de Sobral (SCMS) no setor de Quimioterapia, participei do programa de monitoria na disciplina de Patologia Humana e fui integrante do Projeto de Extensão Humanização Hospitalar. Assim como, desenvolvi ações em educação e saúde como extensionista para pacientes parturientes no hospital Santa Casa de Sobral (SCMS). Pós-Graduanda em Urgência e Emergência pela Universidade Cândido Mendes – UCAM.

Agência Brasileira do ISBN
ISBN 978-85-7247-414-6