



## Review Article

# Classification of mucinous appendiceal neoplasm and pseudomyxoma peritonei

Ghosh Arnab<sup>1</sup><sup>1</sup>Department of pathology, Manipal College of Medical Sciences, Pokhara, Nepal**Keywords:**

Adenocarcinoma;  
 Adenomucinosi;  
 cystadenoma;  
 Appendix;  
 Mucocele;  
 Non-mucinous;

**ABSTRACT**

Mucinous appendiceal tumors are uncommon and include a wide spectrum of tumors whose classification remained controversial. Some of these mucin producing appendiceal tumors can disseminate to the peritoneal cavity leading to pseudomyxoma peritonei (PMP). Despite several attempts to classify mucinous tumors of appendix and PMP by different authors in the past, no universally accepted classification system was present. The controversial issues were discussed at the 2012 World Congress of the Peritoneal Surface Oncology Group International (PSOGI) in Berlin. A panel of 71 experts from 13 different countries was formed under the lead co-ordinator Norman J. Carr. A total of 4 rounds of questionnaires and one meeting were held. The opinion of the majority was taken into account. Importance of intactness of muscularis mucosae, pushing invasion and infiltrative invasion were emphasized. The entities Low grade appendiceal mucinous neoplasm (LAMN) and High grade appendiceal mucinous neoplasm (HAMN) were defined. The terminologies suggested for Goblet cell carcinoid and adenoneuroendocrine carcinoma were goblet cell tumor and adenocarcinoma ex goblet cell carcinoid. Acellular mucin in peritoneum was not classified under PMP which was classified into 3 categories depending upon low grade, high grade cytologic features and presence of signet ring cells. It was suggested to report the extent of mucin and cells separately. A reporting format solely for mucinous appendiceal tumors was formulated by the panel. However, there are some grey areas which may have to be addressed in future.

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**INTRODUCTION**

Primary appendiceal tumors are found in less than 2% of surgically removed appendix and include a wide spectrum of mucinous tumors which pose problems to both pathologist and clinicians as their nature and classification remained controversial.<sup>1</sup> These tumors often cause accumulation of mucin in the appendiceal lumen leading to cystic dilation of appendix. Some of these mucin producing appendiceal tumors can disseminate to the peritoneal cavity leading to pseudomyxoma peritonei (PMP) despite the lack of classic infiltrative pattern of invasion and cellular atypia. And in most PMPs, the cells found in the peritoneal mucin pool are bland in appearance.<sup>1,2</sup> Though since 1960s, these seemingly non-invasive and innocuous tumors were suspected as malignant, most reports before 2000 were of not much value in assessing the biological nature of different types of mucinous appendiceal tumors.<sup>1,2</sup>

### Reporting Checklist for Appendiceal Mucinous Neoplasia and/or Pseudomyxoma Peritonei

Material in *italics* is optional and may be more relevant to research rather than routine reporting. Note that the primary neoplasm and the peritoneal metastases are assessed separately.

#### Patient Details

Hospital Number	Name	DoB	Sex
Clinician	Sample Date	Consent form	

#### Clinical Details

Primary site	<input type="radio"/> Appendix <input type="radio"/> Other (state) _____ <input type="radio"/> Unknown		
Previous appendectomy?	<input type="radio"/> Yes: Date: _____ Diagnosis: _____ <input type="radio"/> Appendix entirely sampled? <input type="radio"/> Yes <input type="radio"/> No <input type="radio"/> Not known <input type="radio"/> No <input type="radio"/> Not known		
Previous mucinous tumor (other than in appendix)?	<input type="radio"/> Yes: Site: _____ Date: _____ Diagnosis: _____ <input type="radio"/> No <input type="radio"/> Not known		
Previous cytoreductions?	<input type="radio"/> Yes: Number of operations: _____ <input type="radio"/> No <input type="radio"/> Not known		
Neoadjuvant therapy?	<input type="radio"/> Yes Type _____ <input type="radio"/> No		
Clinical history and operative findings:	_____		
Cytoreduction:	<input type="radio"/> CC-0 (no visible disease) <input type="radio"/> CC-1 (nodules <2.5 mm) <input type="radio"/> CC-2 (nodules 2.5 mm - 25 mm) <input type="radio"/> CC-3 (nodules >25 mm)	Peritoneal cancer index (PCI) _____ Confined to one quadrant? <input type="radio"/> Yes (state which _____) <input type="radio"/> No <input type="radio"/> Not known / Not applicable	
Organs submitted:	<input type="radio"/> Appendix <input type="radio"/> Greater Omentum <input type="radio"/> Lesser Omentum <input type="radio"/> Right Colon <input type="radio"/> Transverse colon <input type="radio"/> Left Colon <input type="radio"/> Sigmoid <input type="radio"/> Rectum <input type="radio"/> Anus <input type="radio"/> Subtotal colon <input type="radio"/> Other: _____	<input type="radio"/> Small bowel <input type="radio"/> Gallbladder <input type="radio"/> Liver segment <input type="radio"/> Stomach (partial) <input type="radio"/> Stomach (total) <input type="radio"/> Spleen <input type="radio"/> Right Ovary <input type="radio"/> Left Ovary <input type="radio"/> Uterus <input type="radio"/> Umbilicus	Peritonectomies: <input type="radio"/> Right Parietal <input type="radio"/> Left Parietal <input type="radio"/> Pelvic <input type="radio"/> Right Diaphragmatic <input type="radio"/> Left Diaphragmatic <input type="radio"/> Liver Capsule <input type="radio"/> Falciiform ligament <input type="radio"/> Omental bursa
Tumor bank:	<input type="radio"/> Yes: <input type="radio"/> No <input type="radio"/> Not known		

Figure 1: Reporting format for mucinous tumors of appendix as recommended by the PSOGI group<sup>14</sup>

## HISTORICAL ASPECT

Several attempts towards classifying mucinous tumors of appendix and PMP have been made in the past. Woodruff R et al. in 1940 classified 146 cystic tumors of the appendix into mucocele and Adenocarcinoma Grade I.<sup>3</sup> However with time, various opinions, proposals and terminologies came up by different authors. Disputes continued about the nature and nomenclature of these tumors, classification of degree of dysplasia, if present and in case mucin is seen in the appendiceal wall, whether to call the lesion malignant or not. The term appendiceal mucocele and cystadenoma was frequently used by many pathologists though the exact definition of the conditions were uncertain.<sup>4</sup> Some of the authors also used confusing terms like adenomucinosis, borderline tumor of appendix, mucinous tumors of low malignant potential, low grade appendiceal mucinous neoplasm etc.<sup>2,5-7</sup> Disagreement also continued whether the term "PMP" should be used only for macroscopic ascites or on histologic basis or whether it should be used at all or not.<sup>2,7-11</sup> However the term PMP is included in 2010 WHO classification of tumors of the digestive system.<sup>11</sup> Some of the classifications are presented in Table 1 to show the differences in the terminologies used.<sup>1,7,9-13</sup>

#### Macroscopic Description of specimen:

#### Block key:

#### Microscopic

##### PRIMARY SITE

- Appendix  
 Other (give details in comments section): \_\_\_\_\_  
 Primary site not included in specimen

##### APPENDIX (if present)

Type of appendiceal tumor, if present (indicate all that apply): <input type="radio"/> Adenoma (State type: _____) <input type="radio"/> Low grade appendiceal mucinous neoplasm (LAMN) <input type="radio"/> High grade appendiceal mucinous neoplasm (HAMN) <input type="radio"/> Mucinous adenocarcinoma* <input type="radio"/> Non-mucinous adenocarcinoma (colorectal type) <input type="radio"/> Goblet cell carcinoid (GCC) <input type="radio"/> Mucinous goblet cell carcinoid* <input type="radio"/> Adenocarcinoma ex GCC, mucinous* <input type="radio"/> Adenocarcinoma ex GCC, non-mucinous <input type="radio"/> Neuroendocrine tumor (other than GCC)** <input type="radio"/> Other: _____	For carcinomas: <input type="radio"/> Well differentiated (G1) <input type="radio"/> Moderately differentiated (G2) <input type="radio"/> Poorly differentiated (G3) <input type="radio"/> Undifferentiated (G4)  For neuroendocrine tumors: <input type="radio"/> Neuroendocrine tumor Grade 1 <input type="radio"/> Neuroendocrine tumor Grade 2 <input type="radio"/> Neuroendocrine carcinoma Ki67 cell proliferation index: _____ % Mitoses/10hpf: _____																		
Signet ring cells present? <input type="radio"/> Yes – in mucin pools only <input type="radio"/> Yes – within stroma <input type="radio"/> No	If signet ring cells present: <input type="radio"/> <10% <input type="radio"/> 10% to 50% <input type="radio"/> >50% (signet ring cell carcinoma)																		
Indicate furthest local extent of spread of mucin and cells																			
<table border="0"> <tr> <td>Confined to mucosa</td> <td>MUCIN</td> <td>CELLS</td> </tr> <tr> <td>Submucosa</td> <td><input type="radio"/></td> <td><input type="radio"/></td> </tr> <tr> <td>Muscularis propria</td> <td><input type="radio"/></td> <td><input type="radio"/></td> </tr> <tr> <td>Subserosal fat/mesioappendix</td> <td><input type="radio"/></td> <td><input type="radio"/></td> </tr> <tr> <td>Beyond serosa (visceral peritoneum)</td> <td><input type="radio"/></td> <td><input type="radio"/></td> </tr> <tr> <td>Directly invades adjacent structures</td> <td><input type="radio"/></td> <td><input type="radio"/> (specify: _____)</td> </tr> </table>		Confined to mucosa	MUCIN	CELLS	Submucosa	<input type="radio"/>	<input type="radio"/>	Muscularis propria	<input type="radio"/>	<input type="radio"/>	Subserosal fat/mesioappendix	<input type="radio"/>	<input type="radio"/>	Beyond serosa (visceral peritoneum)	<input type="radio"/>	<input type="radio"/>	Directly invades adjacent structures	<input type="radio"/>	<input type="radio"/> (specify: _____)
Confined to mucosa	MUCIN	CELLS																	
Submucosa	<input type="radio"/>	<input type="radio"/>																	
Muscularis propria	<input type="radio"/>	<input type="radio"/>																	
Subserosal fat/mesioappendix	<input type="radio"/>	<input type="radio"/>																	
Beyond serosa (visceral peritoneum)	<input type="radio"/>	<input type="radio"/>																	
Directly invades adjacent structures	<input type="radio"/>	<input type="radio"/> (specify: _____)																	
For appendicectomies: <input type="radio"/> Margin clear (distance: _____ mm) <input type="radio"/> Mucosal neoplasm present at margin <input type="radio"/> Margin not assessable <input type="radio"/> Mural/extra-appendiceal epithelium or mucin present at margin																			

\* Defined by >50% extracellular mucin.

\*\* Using a reporting checklist specifically for neuroendocrine neoplasms is recommended.

Figure 1: Reporting format (Continued) for mucinous tumors of appendix as recommended by the PSOGI group<sup>14</sup>

## PERITONEAL SURFACE ONCOLOGY GROUP INTERNATIONAL

The controversial issues were discussed at the 2012 World Congress of the Peritoneal Surface Oncology Group International (PSOGI) in Berlin. There it was proposed that a consensus method should be developed by a panel of experts. In that process, 71 international experts comprising 34 pathologists along with surgeons and medical oncologists from 13 different countries were included and invited to join the panel. The aim of the process was to develop a consensus on the terminology of PMP and appendiceal neoplasms including goblet cell carcinoid but excluding other tumors with neuroendocrine differentiation. The lead co-ordinator was Norman J. Carr and a modified Delphi approach was adopted for the study. The whole process included round 1 questionnaires to each participating panel expert. At the end of round 1, it was found that 6 different classifications of PMP and 12 distinct classifications for appendiceal lesions were in use by panel members. Furthermore it was noted that the same lesion may have been interpreted by different panel member in different way. So not only there were wide range of terminologies, even a single lesion is called as different entities by the panellists. Round 1 was followed by a 2 day conference in 2013 in UK which was participated by all the panel members. The result of round 1 was discussed

**Table 1: Different terminologies used by different authors in the past<sup>1</sup>**

Comparisons Among Classification Schemes for Appendiceal Mucinous Neoplasms and Pseudomyxoma Peritonei							
		Carr et al, <sup>11</sup> 2010	Misdraji et al, <sup>15</sup> 2003	Pai et al, <sup>17</sup> 2009	Ronnett et al, <sup>1</sup> 1995	Bradley et al, <sup>12</sup> 2006	AJCC 1 2007, <sup>11</sup> 2010
<b>Tumor confined to appendix Limited to mucosa</b>	Low-grade cytology	Adenoma	Low-grade appendiceal mucinous neoplasm	Adenoma	NA	NA	Adenoma
	High-grade cytology	Adenoma	Noninvasive mucinous cystadenocarcinoma	Adenoma	NA	NA	Adenoma
	Positive surgical margin	Adenoma	Low-grade appendiceal mucinous neoplasm	Uncertain malignant potential	NA	NA	Adenoma
	Neoplastic epithelium in appendix wall	Uncertain malignant potential	Low-grade appendiceal mucinous neoplasm	Uncertain malignant potential	NA	NA	Invasive Mucinous Adenocarcinoma
<b>Tumor beyond appendix</b>	Low-grade epithelium in peritoneal mucin	Invasive mucinous adenocarcinoma	Low-grade appendiceal mucinous neoplasm	High-risk for recurrence	Disseminated peritoneal adenomucinosis	Low-grade mucinous carcinoma peritonei	Low-grade mucinous adenocarcinoma
	High-grade epithelium in peritoneal mucin	Invasive mucinous adenocarcinoma	Invasive mucinous adenocarcinoma	Invasive mucinous adenocarcinoma	Peritoneal mucinous carcinomatosis	High-grade mucinous carcinoma peritonei	High-grade mucinous adenocarcinoma

in the above conference. This was followed by further round 3 and round 4 questions to minimize the differences in opinion and to come to a conclusion. For contentious issues, a two third majority was taken as consensus and for non-contentious issues, a simple majority was accepted.<sup>14,15</sup>

### Epithelial Appendiceal Neoplasms

PSOGI panel classified non-carcinoid epithelial neoplasia of the appendix into following subtypes. (Table 2)

- Adenoma (with low grade / high grade dysplasia)
- Serrated polyp (with low grade / high grade dysplasia)
- Low grade appendiceal mucinous neoplasm (LAMN)
- High grade appendiceal mucinous neoplasm (HAMN)
- Mucinous adenocarcinoma
- Mucinous adenocarcinoma with signet ring cells
- Signet ring cell carcinoma
- Non –mucinous adenocarcinoma

### Adenoma

Adenomas typically occur in fifth decade and are more common in females.<sup>4,16,17</sup> Grossly, mucin is absent on the external serosal surface. Appendix may or may not be dilated and on cut up, lumen may show presence of mucin. On microscopy, adenomatous hyperplasia is seen and, by definition, muscularis mucosae must be intact and there must not be any mucin and invasion in the appendicular wall or through the appendicular wall. Similar to the colorectal adenomas, it may be villous or tubular or tubulovillous and may show low grade or high grade dysplasia. Appendicular adenomas are more commonly of villous type in contrast to colonic adenomas and often show circumferential involvement. The main differentials include retention cyst and LAMN. Retention cysts usually show attenuation of epithelium while papillary architecture with tall mucinous cells indicates neoplastic epithelium of adenoma. The main differentiating point from LAMN is presence of an intact muscularis mucosae in adenomas.<sup>1,4,14,19</sup> The terms “cystadenoma” of appendix should no longer be used.<sup>14</sup>

### Serrated polyps

It is similar to the colorectal counterpart with serrated features. Similar to the adenomas, the muscularis mucosae is intact. It may show low grade or high grade dysplasia. The term “serrated polyp” was preferred by the panel over other alternative terms as “sessile serrated adenoma”.<sup>14</sup> In

**Table 2: Classification of mucinous epithelium neoplasm of appendix and their microscopic features**

Microscopic features		Diagnosis
<ul style="list-style-type: none"> <li>Invasion absent</li> <li>Intact muscularis mucosae</li> </ul>	Resembles colorectal adenoma	Adenoma - with/without dysplasia, - low / high grade
	With serrated features	Serrated polyp -with/without dysplasia, -low / high grade
Any of the following - <ul style="list-style-type: none"> <li>Pushing invasion (expansile growth) and desmoplasia absent</li> <li>Loss of muscularis mucosae</li> <li>Fibrosis of submucosa</li> <li>Dissection of acellular mucin in wall</li> <li>Undulating or flattened epithelial growth</li> <li>Rupture of appendix</li> <li>Mucin ( acellular or with cells) outside appendix</li> </ul>	Low grade cytologic atypia	Low grade appendiceal mucinous neoplasm (LAMN)
	High grade cytologic atypia	High grade appendiceal mucinous neoplasm (HAMN)
<ul style="list-style-type: none"> <li>Infiltrating invasion</li> <li>Desmoplastic stroma present (see text for definition)</li> </ul>	Mucin constitute >50%	Mucinous adenocarcinoma (well, moderately , poorly differentiated)
	signet ring cells present <50%	Mucinous ( poorly differentiated ) adenocarcinoma with signet ring cells
	signet ring cells present >50%	Mucinous Signet ring cell carcinoma
Mucin constitute < 50%	Resembles colorectal type	Adenocarcinoma , well , moderately , poorly differentiated

the context, it is noteworthy that these lesions have different mutations to their colonic counterparts, suggesting they are different type of neoplastic proliferation.<sup>18</sup>

#### Low Grade Appendiceal Mucinous Neoplasm (LAMN)

Usual age of presentation is sixth decade and is seen more in females.<sup>7,12</sup> Approximately 25-30% LAMN are incidental finding and majority present as acute appendicitis.<sup>15</sup> Grossly, mucin may or may not be seen on the serosal surface. On microscopy, the main feature is destruction of muscularis mucosae due to “pushing invasion” by the neoplastic epithelium and /or mucin. The epithelium show low grade dysplasia. Submucosa and muscularis propria may show fibrosis, hyalinisation or attenuation, but typical features of infiltrative invasion and desmoplasia (see below) are absent. The fibrosis is typically characterized by small scattered bland fibroblasts in a dense collagenous, often hyalinised matrix. The neoplastic epithelium may push into or even through the wall as diverticulum.<sup>14,19</sup> The differentials include adenoma, serrated polyps, HAMN (see below) and mucinous adenocarcinoma (see below). It is to be noted that any tumor with mucin and / or epithelium dissecting through the wall should not be called as adenoma. To differentiate LAMN from a ruptured adenoma may be difficult and may require several sections to find the pushing invasion by the neoplastic epithelium and low grade cytologic atypia.<sup>14,19</sup>

#### High Grade Appendiceal Mucinous Neoplasm (HAMN)

In HAMN all the features are similar to LAMN except that the cytologic atypia is of high grade. HAMN is a rare entity. This terminology is not included in WHO classification 2010.<sup>11</sup> Later, it was proposed by the PSOGI panel and was also included in American Joint Committee on Cancer (AJCC) Cancer staging manual 8th edition as well as in College of American Pathologists (CAP) protocol.<sup>19,20</sup> It has to be differentiated from LAMN by the degree of cytological atypia and from mucinous adenocarcinoma by the absence of infiltrative invasion.

#### Mucinous adenocarcinoma (MA)

In MA, the main feature is infiltrative invasion and desmoplasia of the stroma. MA may be well, moderately or poorly differentiated depending on cytological atypia. Infiltrative invasion has been defined as tumor budding (infiltration of single individual cells or clusters of up to 5 cells) and / or small irregular glands with frequent angulations. Desmoplastic stroma has been defined as proteoglycan rich extracellular matrix with activated fibro and myofibroblasts with vesicular nuclei. It has to be differentiated from the fibrosis and hyalinisation of submucosa and / or muscularis propria often seen in LAMN and High Grade Appendiceal Mucinous Neoplasm .<sup>4,14,19</sup>

Mucinous adenocarcinoma of appendix accounts for about 40% of all appendiceal adenocarcinomas. They

Other findings:  
 Diverticulum (Site: tip / body / base)  
 Extensive epithelial denudation  
 Suppurative appendicitis  
 Mural fibrosis  
 Perforation through tumor (Site: tip / body / base)  
 Perforation away from tumor (Site: tip / body / base)  
 Other lesion: \_\_\_\_\_

Other features of tumor (optional):  
 Architectural pattern(s):  
 Flat strips of epithelium  
 Villiform/papillary with fibrovascular cores  
 Serrated  
 Cribriform  
 Single cells or small clusters in mucin pools  
 Pushing, broad-front, expansile invasion  
 Infiltrative, desmoplastic (classic) invasion  
 Tumor budding/discohesive cells at invasion front  
 Other: \_\_\_\_\_

Cytologic atypia:  
 None  
 Minimal  
 Moderate  
 Marked (high grade)  
 Not assessable

Mitotic activity:  
 Rare (0-2/10hpf)  
 Occasional (3-5/10hpf)  
 Abundant (>5/10hpf)  
 Not assessable

**NODES**

Site	Number examined	Number involved	Site	Number examined	Number involved
Mesoappendix			Omentum (gastro-epiploic)		
Right mesocolon			Stomach		
Left mesocolon			Spleen		
Other nodal basins (specify) _____					
Summary:		Regional nodes:	<input type="checkbox"/> Positive <input type="checkbox"/> Negative <input type="checkbox"/> Not assessed		
		Non-regional nodes:	<input type="checkbox"/> Positive <input type="checkbox"/> Negative <input type="checkbox"/> Not assessed		

**VASCULAR AND PERINEURAL INVASION**

Lymphovascular:  Yes  No  
 Perineural:  Yes  No

**PERITONEAL DISEASE (includes omentum)**

Mucinous disease involving peritoneum?  
 Yes  No

If yes, overall classification:  
 Low grade mucinous carcinoma peritonei / DPAM (disseminated peritoneal adenomucinosis)  
 High grade mucinous carcinoma peritonei with signet ring cells / PMCA-S  
 Percentage of signet ring cells, if present:  <10%  10-50%  >50%

For appendiceal primaries:  
 Spread of acellular mucin:  
 Acellular mucin confined to vicinity of appendix  
 Acellular mucin beyond the right lower quadrant  
 Spread of epithelial cells:  
 Epithelial cells confined to vicinity of appendix  
 Epithelial cells beyond the right lower quadrant

Figure 1: Reporting format (Continued) for mucinous tumors of appendix as recommended by the PSOGI group<sup>14</sup>

Other neoplasm involving peritoneum?  
 Yes  No

If yes, type:  
 Goblet cell carcinoid  
 Adenocarcinoma ex-goblet cell carcinoid  
 Neuroendocrine tumor grade 1  
 Neuroendocrine tumor grade 2  
 Non-mucinous adenocarcinoma  
 Other: \_\_\_\_\_

Additional cellular features, if cells are present (optional):  
 Cytologic atypia:  
 None  
 Minimal  
 Moderate  
 Marked (high grade)  
 Rare (0-2/10hpf)  
 Occasional (3-5/10hpf)  
 Abundant (>5/10hpf)  
 Not assessable

Architectural pattern:  
 Flat strip  
 Villiform/papillary  
 Serrated  
 Cribriform  
 Single cells or small clusters of cells floating in mucus  
 Signet ring cells – discohesive  
 Signet ring cells in confluent sheets  
 Signet ring cells infiltrating stroma  
 Infiltrative glands with irregular profiles  
 Other: \_\_\_\_\_

Cellularity:  
 Acellular (no epithelial cells)  
 Scant (<2% of mucinous component consists of cells)  
 Moderate (2-19% of mucinous component consists of cells)  
 High (>20% of mucinous component consists of cells)  
 Not assessable

**INVASION OF OTHER ORGANS**

Organ invasion?  
 (This includes any spread into the wall/parenchyma of the organ, whether infiltrative or not.)  
 Yes  
 No  
 Not assessable

If yes, indicate organs involved:  
 Ovary  
 Spleen  
 Large intestinal wall  
 Small intestinal wall  
 Stomach wall  
 Myometrium  
 Other: \_\_\_\_\_

Invasion pattern (indicate most aggressive pattern):  
 Acellular mucin only  
 Pushing, broad-front invasion by epithelium  
 Infiltrative invasion by irregular glands or single cells with desmoplasia; includes tumor budding and discohesive cells at invasion front

**NEOADJUVANT THERAPY**

Neoadjuvant therapy given?  
 Yes  No  Not known

Results of neoadjuvant therapy, if applicable:  
 No significant histologic response  
 Response: \_\_\_\_\_

**TNM code** \_\_\_\_\_

**COMMENTS:** \_\_\_\_\_

**PATHOLOGIST:** \_\_\_\_\_ **DATE:** \_\_\_\_\_

Figure 1: Reporting format (Continued) for mucinous tumors of appendix as recommended by the PSOGI group<sup>14</sup>

can rupture and cause PMP, as well as, can also spread through hematogenous route. Histologically, they can be graded as well, moderately and poorly differentiated. The main differentials include LAMN, HAMN and Goblet cell carcinoma (discussed below). Patients with MA have a better prognosis than those with non-mucinous adenocarcinoma.<sup>1,4,15</sup>

**Mucinous adenocarcinoma with signet ring cells and Signet ring cell carcinoma**

If signet ring cells are seen in the mucinous pool, the percentage of signet ring cells determines the diagnostic terminology. If signet ring cells are less than 50% of the cells, it is called as poorly differentiated mucinous adenocarcinoma with signet ring cells. And if they constitute more than 50% of the cells, it is termed as mucinous signet ring cell carcinoma.<sup>14,19</sup>

**Non-mucinous adenocarcinoma**

This entity is the counter part of traditional adenocarcinoma - colorectal type and can be subtyped as well (>95% gland formation), moderately (50-95% gland formation) or poorly differentiated (<50% gland formation).<sup>19</sup>

**Goblet cell carcinoid**

Goblet cell carcinoids show poorer prognosis than pure appendiceal neuroendocrine tumors.<sup>19</sup> The term Goblet cell carcinoid is well recognised and is present in AJCC 8th edition. However PSOGI panel considered it as misleading and suggested a new name “Goblet cell tumor” which is synonymous. It was further suggested that this entity should be subtyped as mucinous (>50% extracellular mucin) and non-mucinous (<50% extracellular mucin).<sup>14</sup>

Some tumors show a combination of goblet cell carcinoids and adenocarcinoma and behave more aggressively than pure goblet cell carcinoid.<sup>19</sup> These tumors have been named “adenoneuroendocrine carcinoma” in WHO 2010.<sup>11</sup> However AJCC 8th edition and CAP protocol have mentioned that this term may cause a mistaken impression of a poorly differentiated neuroendocrine carcinoma. These tumors are better designated as “mixed goblet cell carcinoid-adenocarcinoma” or “adenocarcinoma ex goblet cell carcinoid”.<sup>14,19-21</sup>

**Pseudomyxoma peritonei (PMP)**

As mentioned above, PMP refers to the accumulation of mucin within the peritoneal cavity secondary to mucinous



epithelial neoplasia mostly of appendiceal origin, namely LAMN and mucinous adenocarcinoma.<sup>4</sup> The usual age of presentation is 6<sup>th</sup> to 7<sup>th</sup> decade and in some series it shows female predilection.<sup>4</sup> It usually shows slow and continuous intra-peritoneal growth but distant metastasis is rare. Generally it originates from the mucinous tumor from the appendix but occasional cases of primary mucinous tumor of other organs including ovary, colon, urachus and pancreas were reported.<sup>1,4</sup>

PSOGI panel defined PMP as intraperitoneal accumulation of mucus due to mucinous neoplasia characterized by redistribution phenomenon. It can include mucinous ascites, peritoneal implants, omental cake and ovarian involvement. It most commonly arises from the appendiceal neoplasia. It was noted that PMP is a clinical syndrome which should be considered malignant and appendiceal lesions with low grade or high grade features can present as PMP.

It was decided by the panel that the peritoneal component and the appendiceal tumor should be reported and termed separately.<sup>14,19</sup>

PSOGI panel classified peritoneal disease component into 4 diagnostic groups viz.,<sup>14,19</sup>

- “Acellular mucin only” is characterised by presence of mucin without epithelial cells. A comment should be added on whether the mucin is confined close to the organ of origin or distant from it. The word PMP should be avoided for this category unless clinically indicated.
- “Low grade mucinous carcinoma peritonei” or “disseminated peritoneal adenomucinosis (DPAM)” is characterized by PMP with low grade histologic features.
- “High grade mucinous carcinoma peritonei” or “peritoneal mucinous carcinomatosis (PMCA)” is characterised by PMP with high grade histologic features. Even focal high grade atypia also should be considered under this category.
- “High grade mucinous carcinoma peritonei with signet ring cells” or “PMCA with signet ring cells (PMCA-S)” is characterised by PMP with signet ring cells.

So, the summary of the PSOGI diagnostic groups is that the term PMP should be used only if cells are present in the mucin and PMP is divided into 3 groups as low grade, high grade and signet ring. These grading schemes are not applicable to poorly differentiated neuroendocrine carcinoma and goblet cell carcinoid.<sup>19,20</sup>

### Reporting Format

The reporting format of CAP addresses all types of appendiceal tumors including mucinous and non-mucinous tumors. The PSOGI group formulated a separate reporting

format meant only for appendiceal mucinous tumors and PMP. It has been provided above for the convenience of the readers. Majority suggested that in PMP, the spread of cells and mucin should be assessed and reported separately (fig.1).<sup>14</sup>

### CONCLUSION

PSOGI has put a great effort to standardize the terminologies related to appendiceal mucinous tumors and PMP. However, still there are several uncertain issues, discrepancies and grey zone areas, which can be addressed in future. There are differences between PSOGI guideline and AJCC 8th edition recommendations. Subjective variations regarding low and high grade dysplasia among different pathologists can occur and differentiating signet ring cells from degenerating tumor cells may become tricky especially if the cellularity is low. Furthermore, all these different conditions and terminologies should have proper therapeutic and prognostic significance, for which further studies with long term follow up are required.

**Conflict of interest:** None

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