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Adenomatoid tumours of the gastrointestinal tract – a case-series and review of the literature

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Aims: Adenomatoid tumours are mesothelial-derived benign neoplasms with a predilection for the genital tract. Extragenital sites are rare and can cause significant diagnostic challenges. Herein, we describe the clinicopathological features of a cohort of adenomatoid tumours involving the gastrointestinal tract and liver in order to more clearly characterise their histological findings and aid in diagnosis.

Methods and results: The pathology databases at four institutions were searched for adenomatoid tumours involving the gastrointestinal tract or liver, yielding eight cases. Available clinicoradiological and follow-up data were collected from the medical records. Six tumours were incidentally discovered during imaging studies or at the time of surgical exploration for unrelated conditions; presenting symptoms were unknown in two patients. Histologically, the tumours were well-circumscribed, although focal ill-defined borders were present in four cases. No infiltration of adjacent structures was identified. Architectural heterogeneity was noted in five (63%) tumours; an adenoid pattern often predominated. The neoplastic cells were flattened to cuboidal with eosinophilic cytoplasm. Cytoplasmic vacuoles mimicking signet ring-like cells were present in five (63%) cases. Three (38%) cases showed involvement of the mesothelium with reactive mesothelial hyperplasia. Cytological atypia or increased mitotic activity was not identified. The surrounding stroma ranged from oedematous/myxoid to densely hyalinised. Immunohistochemistry confirmed mesothelial origin in all cases evaluated. No patients developed recurrence of disease.

Conclusions: The current study evaluates the clinicopathological findings in a collective series of gastrointestinal and hepatic adenomatoid tumours, correlating with those described in individually reported cases. We highlight common histological features and emphasise variable findings that could mimic a malignant neoplasm.

Keywords: adenomatoid tumour, benign neoplasm, gastrointestinal tumour, immunohistochemistry, liver cyst, mesothelial neoplasm peritoneal tumour

Introduction

Adenomatoid tumours are rare, benign mesothelial neoplasms that are most frequently identified within the genital tract.[1–3] Extragenital tract locations have been reported, including tumours within the

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adrenal gland, liver, pancreas, omentum, small bowel mesentery and lymph nodes[4–8]; however, tumours at these sites are uncommon, and a comprehensive search of the literature reveals fewer than 20 gastrointestinal or hepatic adenomatoid tumours. Given their rarity, encountering an adenomatoid tumour in one of these locations can create a significant diagnostic challenge, particularly as these tumours often have a glandular appearance and frequently possess signet ring-like cells, mimicking adenocarcinoma. However, the distinction is of utmost importance as these tumours are benign, typically do not recur after resection and do not require additional therapy.

Our goals were to evaluate the clinical, radiographic and histopathological features in a series of adenomatoid tumours involving the gastrointestinal tract and liver, in order to more clearly characterise key features that will aid in their diagnosis. In addition, an extensive literature search was performed to summarise the findings in previously reported cases. Increased awareness of this uncommon entity in unusual sites and recognition of certain histological clues will help to avoid potential diagnostic pitfalls

Table 1. Clinical and radiologic/intraoperative features in 8 adenomatoid tumors of the gastrointestinal tract and liver

Case	Sex	Age (years)	Clinical Presentation	Underlying immune status	Location	Size (cm)	Radiologic/ Intraoperative Characteristics	Follow-up Interval (months)
1	F	33	N/A	Immunocompetent	Liver and retroperitoneum	15	Multiloculated cyst involving segments 4/5 and extending into retroperitoneum	4
2	F	52	N/A	N/A	Right colon mesentery	3	Mesenteric mass near appendix	N/A
3	M	42	Incidental finding on imaging for persistent back/flank pain	Immunocompetent	Splenic flexure mesentery	2.1	Firm mass within the omentum abutting splenic flexure	1
4	F	39	Incidental finding during resection for Crohn disease	Immunosuppressed (medically refractory Crohn disease)	Greater omentum	2.2	Fleshy mass in greater omentum overlying ileum	29
5	M	72	Incidental finding during abdominal exploration	Immunocompetent	Abdominal peritoneum	1.4	Mucinous appearing implant	128
6	F	57	Incidental finding during abdominal exploration	Immunocompetent	Serosa of ileum	0.2	Firm nodule	14
7	M	40	Incidental finding during resection for Crohn disease	Immunosuppressed (medically refractory Crohn disease)	Detached fat with nodule in ileal resection specimen	0.8	Inflammatory changes/fibrotic tissue	N/A
8	F	65	Incidental finding during surgery (total abdominal hysterectomy, bilateral salpingo-oophorectomy, debulking) for high grade serous carcinoma of ovary	Immunocompromised (neoadjuvant chemotherapy for ovarian carcinoma)	Perigastric tissue	0.2	Nodule, NOS	N/A

F, Female; M, Male; N/A, Not applicable.

and guide the use of immunohistochemistry to facilitate an accurate diagnosis.

Methods

With institutional review board approval at the University of Michigan, we retrospectively reviewed the pathology databases from participating institutions to identify adenomatoid tumours that were diagnosed on the gastrointestinal pathology service due to the clinical presentation and/or an association with the gastrointestinal/hepatobiliary tract. Search terms included gastrointestinal or hepatobiliary specimens with 'adenomatoid tumour' or 'adenomatoid' in the diagnosis over a variable range, spanning years 2000 to 2021. Information regarding clinical presentation, underlying immune status, imaging features and intraoperative findings were obtained from the electronic medical records when available. Routinely processed, haematoxylin and eosin (H&E)-stained slides were evaluated by a pathologist at each institution. In addition, at least one representative virtual slide from each case was centrally reviewed at a single institution (University of Michigan, Ann Arbor, MI, USA) by three additional pathologists (E.H., J.S., L.W.L.). Each case was assessed for histological characteristics, including predominant morphological patterns (adenoid, angiomatoid, cystic or solid), border configuration, involvement of surrounding organs/structures, presence of signet ring-like cells, stromal features, associated lymphoid aggregates and presence of necrosis/infarction. Follow-up information was obtained for each patient when available.

Results

Eight cases of adenomatoid tumour involving the gastrointestinal and/or hepatobiliary tract were identified from eight unique patients, including five females and three males. Clinical and radiological features are listed in Table 1.

All patients were adults, with a mean age of 50 years (range = 33–72 years). All six tumours for which information was available regarding the patient's initial presenting symptoms were identified incidentally, five at the time of surgery and one during imaging studies performed for unrelated symptoms. Two patients were transferred from outside institutions due to the presence of a mass detected on imaging studies, but the initial indication for work-up was not available. Of those identified intraoperatively, two patients underwent abdominal surgery because of refractory Crohn disease, one of whom had reportedly failed multiple lines of therapy, including biological agents, eventually necessitating bowel resection. In both of these patients, a grossly identifiable nodule was found intraoperatively, one in the greater omentum and the other in the small bowel mesentery. In three other patients, the tumours were incidental findings during abdominal exploration for other diagnoses and were located in the abdominal peritoneum, perigastric tissue and serosa of the ileum. In one patient, the tumour was an incidental finding in the splenic flexure mesentery on imaging studies for persistent back/flank pain. Another patient presented with an intra-abdominal mass within the right colon mesentery. Lastly, one patient presented from an outside institution with a slowly growing, large 15-cm cystic mass involving the liver and retroperitoneum. Besides Crohn disease in two patients and recent chemotherapy for ovarian carcinoma in one patient, no other patients were known to be immunocompromised.

The pathological features are summarised in Table 2. On gross examination, the tumours ranged from 0.2 to 15 cm (median = 1.75 cm). The gross appearance varied from multilocular and cystic to a fleshy, mucinous or firm solid mass. In general, the tumours were relatively well-circumscribed; however, four of the cases showed some areas with ill-defined borders and extension into adjacent fibroadipose tissue (Figure 1). No cases showed direct infiltration of adjacent structures or organs, including the bowel wall.

Architecturally, the tumours contained heterogeneous growth patterns. Five (63%) cases showed a predominant adenoid morphological pattern comprised of small tubules, trabeculae and/or anastomosing cords lined by bland, flattened to cuboidal epithelium with clear to eosinophilic cytoplasm (Figure 2A), whereas the tumour involving the liver was predominantly cystic with adenoid and angiomatoid foci (Figure 2B). One case within the serosa of the ileum predominantly consisted of solid nests with scattered adenoid foci (Figure 2C), and one case within the right colon mesentery was predominantly angiomatoid with focal adenoid areas (Figure 2D). Additionally, a micropapillary architectural pattern was focally noted in one case (Figure 2E). Cytoplasmic vacuoles mimicking signet ring cells were present in five of the eight cases (63%) (Figure 2F). Overall, while prominent nucleoli were present in two tumours, no significant cytological atypia or mitotic activity were noted in any of the cases.

Table 2. Summary of histopathologic findings in 8 adenomatoid tumors of the gastrointestinal tract and liver

Case No	Histologic pattern – Predominant component	Histologic pattern – minor components	Border configuration	Signet ring-like cells	Lymphoid aggregates	Cytologic features	Stroma
1	Cystic	Adenoid, angiomatoid	Focally ill-defined	Present	Present	Flattened to cuboidal epithelium with eosinophilic cytoplasm	Extensive myxoid/fibrotic stroma with frequent intermixed inflammatory infiltrates and prominent fibroinflammatory reaction surrounding cyst rupture with fibrin/hemorrhage
2	Angiomatoid	Adenoid	Focally ill-defined	Present	Present	Predominantly flattened and focally cuboidal epithelium with eosinophilic, vacuolated cytoplasm	Fibrous stroma with focal edematous/ myxoid areas, hemorrhage, and a mixed inflammatory infiltrate
3	Adenoid	Angiomatoid	Focally ill-defined	Present	Present	Predominantly flattened to slightly plump, cuboidal epithelium with eosinophilic cytoplasm and pinpoint nucleoli; focally intermingles with mesothelial surface, which contains reactive changes	Fibrotic, focally hyalinized stroma with mixed inflammatory infiltrate
4	Adenoid		Well-circumscribed	Absent	Present	Plump cuboidal epithelium with pinpoint nucleoli and eosinophilic cytoplasm; associated with papillary mesothelial hyperplasia	Dense, hyalinized stroma
5	Adenoid	Solid nests	Focally ill-defined	Present	Absent	Predominantly vacuolated signet ring-like cells	Dense, hyalinized stroma
6	Solid		Well-circumscribed	Present	Absent	Syncytial/ill-defined cell borders, eosinophilic cytoplasm, focal papillary mesothelial hyperplasia	Relatively scant hyalinized stroma
7	Adenoid	Cystic, micropapillary, solid	Well-circumscribed	Absent	Absent	Plump epithelioid cells with prominent nucleoli and abundant eosinophilic cytoplasm	Myxoid to fibrous stroma
8	Adenoid		Well-circumscribed	Absent	Absent	Flattened to cuboidal epithelium with eosinophilic cytoplasm	Dense, hyalinized stroma

The tumour stroma was often prominent, and ranged from loose, oedematous and focally myxoid (Figure 3A) to fibrotic and hyalinised with thick collagen bands interspersed between the tumour nests (Figure 3B). Of note, the large multicystic lesion adjacent to the liver contained frequent areas of cyst rupture with an expansile, fibroinflammatory reaction within the tumour (Figure 3C). Surrounding

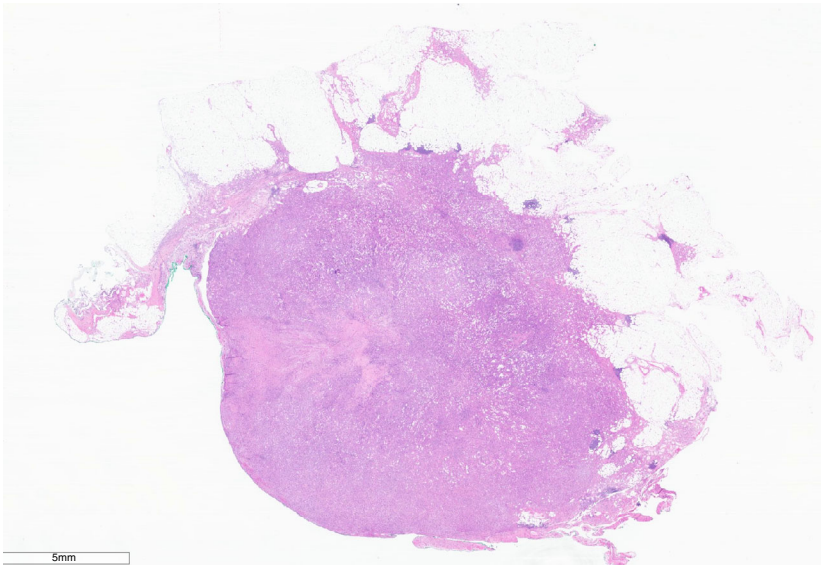

Figure 1. An adenomatoid tumour identified within the right colon mesentery shows a relatively well-circumscribed nodule. However, focal ill-defined extensions of lesional cells within a dense stroma are seen infiltrating into the surrounding fibroadipose tissue as linear extensions and detached small aggregates.

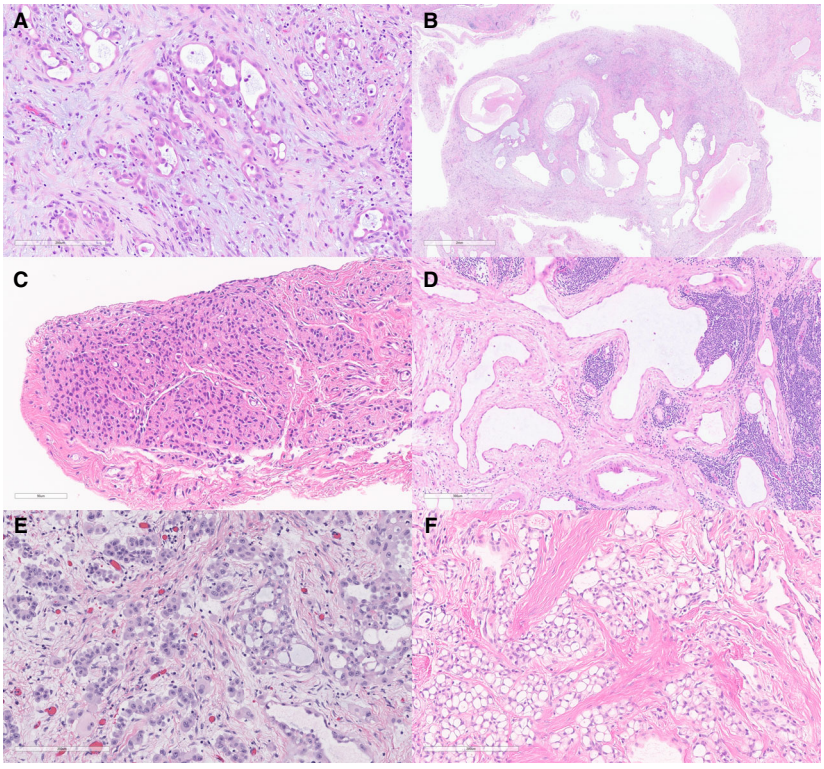

Figure 2. Adenomatoid tumours show significant architectural heterogeneity with most tumours predominantly harbouring an adenoid pattern comprised of small tubules and interanastomosing cords lined by flattened to slightly cuboidal epithelium with eosinophilic cytoplasm and bland nuclei (**A**). Some cases contained large cystic structures, particularly within the liver lesion (**B**), whereas solid nests (**C**) and angiomatoid (**D**) structures were more common in others. One case with predominant adenoid morphology also harboured micropapillary structures lined by cuboidal epithelium with prominent nucleoli (**E**). Prominent intracytoplasmic vacuoles mimicking signet ring cells were noted in most cases (**F**).

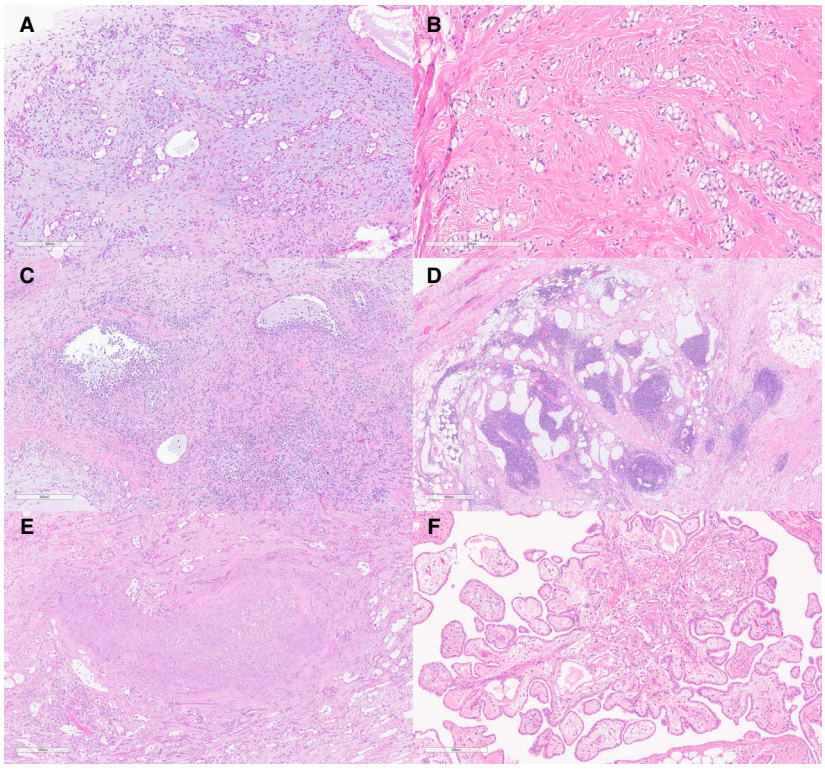

Figure 3. Adenomatoid tumours often harboured a prominent stromal component with variable features. Several cases contained an oedematous to myxoid stroma (**A**). Dense, hyalinised stroma was also a common finding (**B**). Cases with predominant angiomatoid or cystic architecture showed evidence of cyst rupture with an exuberant associated inflammatory infiltrate (**C**). Lymphoid aggregates at the periphery of the tumour were frequent (**D**). One case showed a localised infarction (**E**). Papillary mesothelial hyperplasia was noted in three tumours in which the lesional tissue focally involved the surface mesothelium, mimicking a well-differentiated papillary mesothelioma (**F**). [Colour figure can be viewed at wileyonlinelibrary.com]

lymphoid aggregates were noted in four cases (50%) (Figure 3D). Focal infarction was present in one case (Figure 3E). Three cases were intimately associated with papillary mesothelial hyperplasia of the overlying mesothelium, one of which was quite exuberant (Figure 3F).

Immunohistochemical staining results were available in seven of the above cases for confirmation of mesothelial origin (the seventh case did not have sufficient material for ancillary testing, and thus the diagnosis was rendered based on the morphological features alone). All seven cases were positive for calretinin and five cases underwent additional staining, including pancytokeratin and Wilms tumour (WT1), which were uniformly positive (Figure 4C,D). BRCA1-associated protein 1 (BAP1) was performed in four cases, all of which were retained (Figure 4E).

Follow-up information was available for five patients. The follow-up interval for these patients ranged from 1 to 128 months (median = 14 months). All patients had no evidence of residual or recurrent disease at the most recent follow-up.

Discussion

The purpose of this study was to review the clinical and histological spectrum of adenomatoid tumours arising in gastrointestinal and hepatic locations in order to raise awareness among pathologists of adenomatoid tumours in these uncommon sites. To our knowledge, this is the largest series of gastrointestinal and hepatic adenomatoid tumours. We highlight common histological features that may aid in establishing the correct diagnosis, including the presence of relatively well-circumscribed, non-infiltrative borders, predominant adenoid morphology with some architectural heterogeneity, bland flat to cuboidal epithelium with eosinophilic cytoplasm and a prominent stromal response. Our study also emphasises that variably present histological features, including angiomatoid, cystic, papillary or signet ring cell foci, may lead to confusion with other, often malignant entities that occur in these locations. Once suspected, the appropriate use of immunohistochemical stains can be utilised to confirm the diagnosis.

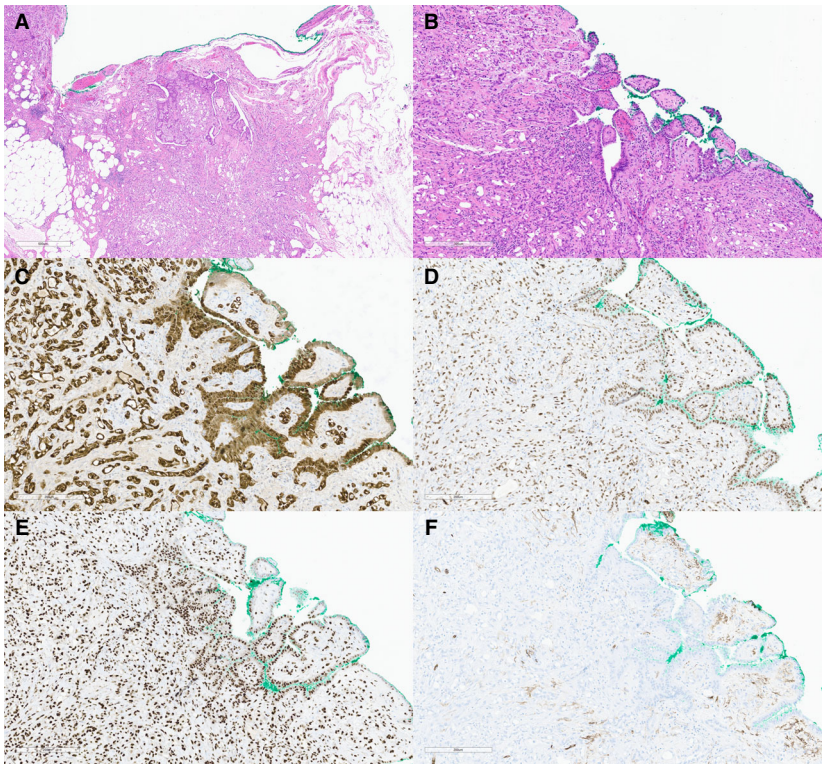

Figure 4. Low-power view of an adenomatoid tumour extending to the mesothelial-lined surface of the mesentery with associated papillary mesothelial hyperplasia (**A**,**B**). Immunohistochemical stains confirm that the lesional cells display the same immunophenotype as the overlying mesothelium, with diffuse positivity for calretinin (**C**) and Wilms tumour 1 (WT1) (**D**). BRCA1-associated protein 1 (BAP1) is retained in both the lesional cells as well as the hyperplastic mesothelium (**E**). A CD34 immunostain is negative (**F**). [Colour figure can be viewed at wileyonlinelibrary.com]

Adenomatoid tumour, initially named by Golden et al. in 1945 when they published the first case-series, is a benign tumour thought to be of mesothelial origin.[9] While most reported cases involve the male and female genital tracts, with the epididymis, uterus and fallopian tubes being common sites, rare extragenital tumours have also been described in the literature. Multiple case reports and small case-series have identified adenomatoid tumours within the adrenal gland,[4,10,11] whereas even rarer isolated case reports have documented involvement of other sites including the heart, pleura, lymph nodes and peritoneum.[5–7,12]

Both the mesothelial origin and the neoplastic (albeit clinically indolent) nature of these lesions have been a source of controversy in the past; however, there is now substantial evidence in support of both. Early ultrastructural evidence initially suggested mesothelial derivation,[13–16] which was later supported by immunohistochemical studies.[3,17] Clonality was assessed by Wang et al. by utilising patterns of X chromosome inactivation in 13 uterine adenomatoid tumours, which showed uniform non-random patterns consistent with monoclonality in all informative cases.[18] Another study evaluating uterine adenomatoid tumours found block-like positivity for p16 in >90% of their cases.[19] More recent molecular studies of adenomatoid tumours have identified *TRAF7* mutations, although the frequency in the few studies evaluating this alteration has ranged significantly from 8 to 100% of cases.[19–21]

The first adenomatoid tumour involving the gastrointestinal tract was reported by Craig et al. in 1979, in which they described a 2-cm nodule within the small intestinal mesentery that was incidentally discovered at the time of laparotomy. In this case report, the nodule was initially misclassified as a metastatic adenocarcinoma.[12] To date, there have been <20 adenomatoid tumours involving the gastrointestinal tract reported in the literature, including one in the pancreas, six involving omentum or mesentery with variable intestinal wall involvement, five involving the liver and one within the appendix (Table 3).[7,12,22–32] However, the true incidence of adenomatoid tumours involving the gastrointestinal tract is difficult to ascertain, as many of these lesions may have been misclassified on final diagnosis, possibly as other benign entities or mesothelial lesions

Table 3. Summary of reported adenomatoid tumors involving the gastrointestinal tract and liver in the literature

Case Report (First author, year)	Sex	Age	Size (cm)	Solitary/ Multiple	Presentation	Location	Histologic Features
Craig JR et al., 1979[12]	M	39	2	solitary	incidental at time of laparotomy	small intestine mesentery	Bland, uniform nuclei focally merging with surface mesothelium surrounded by lymphoid aggregates; collagenous fibrous stroma
Lao IW et al., 2014[22]	F	44	5	solitary	abdominal pain, partial small bowel obstruction	small bowel (transmural)	Variably sized tubules lined by bland epithelioid cells
Yeh CJ et al., 2008[7]	F	47	1.5–2.5 (omental nodules), 8 (mesocolon)	multiple	incidental at the time of laparotomy	mesocolon and omentum	Tubules and anastomosing channels lined by flattened to cuboidal cells within an edematous stroma
Hayes SJ et al., 2007[23]	F	74	0.2 (peritoneal nodule), 0.5 (liver)	multiple	incidental at the time of staging laparoscopy	liver and peritoneum	Angiomatoid architecture lined by epithelioid cells, some of which had vacuolated cytoplasm, within a fibrous stroma
Hanada S et al., 2003[24]	F	26	N/A	multiple	incidental at the time of laparotomy for large endometrial adenomatoid tumor	appendix	Cystic and glandular spaces lined by flattened to cuboidal cells within connective tissue septa
Nagata S et al., 2008[25]	M	39	2	solitary	incidentally detected by radiography	liver	Cystic/angiomatoid spaces lined by cuboidal to flattened epithelioid cells surrounded by fine collagenous bands
Overstreet K et al., 2003[26]	F	58	1.7	solitary	incidentally detected by radiography	pancreas	Solid aggregates, nests, and small glands lined by attenuated cuboidal cells within a collagenous stroma and surrounding lymphocytic aggregates
Van Seventer I et al., 2014[27]	M	51	15	solitary	abdominal pain	liver	Multicyclic tumor lined by epithelioid cells, some of which vacuolated cytoplasm surrounded by variable fibrosis and hemorrhage

Table 3. (*Continued*)

Case Report (First author, year)	Sex	Age	Size (cm)	Solitary/ Multiple	Presentation	Location	Histologic Features
Adachi S et al., 2012[28]	M	58	3	solitary	detected by radiography	liver	Variably dilated tubules lined by flattened to plump epithelioid cells and signet ring-like tumor cells within an edematous to collagenous stroma, some of which showed papillary projections
Hatano Y et al., 2011[29]	M	45	2.8	solitary	incidentally detected by radiography	omentum	Irregular cysts lined by flattened to epithelioid cells; minor separate component with prominent papillary protrusions lined by cuboidal cells (histologically compatible with WDPM)
Skafida E et al., 2013[30]	F	32	2	solitary	incidental at the time of laparotomy	omentum	Cysts and tubules/glands lined by flattened to cuboidal cells, many of which contained vacuolated cytoplasm surrounded by a loose to dense stroma with hyalinization
Ruiz-Tovar et al., 2011[31]	F	48	N/A	solitary	gastrointestinal bleeding	peritoneum with transmural ileocecal involvement	Solid areas and tubules lined by flattened cells
Grosse-Holz M et al., 2013[32]	F	64	3	solitary	incidentally detected by radiography	liver	Small cavities lined by epithelioid cells within a collagen rich connective tissue and scattered lymphocytic aggregates

F, Female; M, Male; N/A, Not applicable.

not further subclassified. While most were reportedly single lesions, three of these cases harboured multiple tumours, including one patient with nodules involving both the liver and peritoneum and another patient with multiple tumours in the mesocolon and omentum.[7,23,24] One appendiceal case was identified in association with a 15-cm uterine adenomatoid tumour.[24] Similar to our cohort, most cases were incidental findings; however, a subset of patients presented with symptoms. In particular, two case reports described transmural involvement of the bowel wall (a feature that was not identified in any of our cases). In both of these cases the patients were symptomatic; one patient presented with small bowel obstruction and the other with gastrointestinal bleeding.[22,31] Similar to our case involving the liver, several other reports have documented patients presenting with a radiologically identified cystic mass within the liver.[25,32] Grossly, the size of these tumours has ranged from 0.2 to 15 cm (median = 2 cm). The reported histological features are similar to those seen in the current case-series, with a prominence of adenoid architecture and variable angiomatoid and cystic areas, often with architectural heterogeneity. None of the previous cases of gastrointestinal (GI) or hepatic adenomatoid tumour reported in the literature had evidence of local recurrence or progression of disease.

Interestingly, as was also demonstrated in our cohort, there are two previous reports of omental adenomatoid tumours with an associated proliferative papillary mesothelial process simulating a well-differentiated papillary mesothelioma.[29,33] Another case report described the tumour merging with the overlying surface mesothelium.[12] These findings are notable, as others have documented separate, synchronous adenomatoid tumours and mesothelial lesions within the same patient which has led to some to propose a possible link between adenomatoid tumours and other peritoneal mesothelial lesions, including multicystic mesothelioma and well-differentiated papillary mesothelioma. More recently, the evidence that both adenomatoid tumours and well-differentiated papillary mesotheliomas can harbour *TRAF7* mutations further supports a pathological link between these two entities.[34]

Another interesting finding in our case-series is the association with Crohn disease in two patients harbouring adenomatoid tumours involving the omentum and small bowel mesentery, an association that has not been previously described. Several studies have, however, documented an association between adenomatoid tumours and immunocompromised patients, with tumours previously described in renal transplant patients, acquired immunodeficiency syndromes including human immunodeficiency virus (HIV) and patients with haematolymphoid malignancies.[19,20,35–38] In particular, one study examined 1094 hysterectomies and identified 17 adenomatoid tumours, 10 of which (58.8%) were found in renal transplant patients.[39] Another study evaluating hysterectomy specimens identified adenomatoid tumours in 25% of immunosuppressed patients compared with only 1.52% of non-immunosuppressed patients. In addition, they found that adenomatoid tumours in immunosuppressed patients were often multifocal or diffuse, rather than single nodules.[19] Although this evidence is strongly suggestive of such an association, the exact mechanism of how and why these tumours develop in the immunocompromised setting requires further exploration. Further complicating any conclusions drawn in the current study, the association with Crohn disease in two of our patients may also be related to peritoneal inflammation leading to reactive mesothelial proliferation changes rather than immunocompromised status, an association also well-described with adenomatoid tumours, as noted previously.

While these tumours usually harbour characteristic histological features which aid in their diagnosis, several findings may lead to diagnostic confusion, especially when adenomatoid tumours are encountered in unusual locations. In fact, two of the cases in the current series were initially misclassified on frozen section, and three cases required send-out consultation by the initial pathologist to one of the participating academic institutions for ultimate diagnosis. The epithelial lining of adenomatoid tumours is typically comprised of flattened to cuboidal uniform cells with variable eosinophilic cytoplasm. In some cases, there is striking attenuation of the lining, resembling endothelial cells and mimicking a vascular lesion. Fortunately, immunohistochemistry using vascular markers can help to make the distinction. The glandular morphology, focal areas of irregular growth at the periphery and signet ring-like cells can certainly raise the possibility of a malignant neoplasm, particularly a metastatic adenocarcinoma. This may be particularly challenging when these cases are sent for frozen section evaluation at the time of surgery. Close inspection, however, should reveal a lack of significant cytological atypia or mitotic activity, and immunohistochemical analysis can further confirm the mesothelial nature of the lesional cells. Malignant mesothelioma is also in the differential diagnosis for lesions within the peritoneal cavity, and adenomatoid variants of epithelioid malignant mesothelioma exist. However, more typical patterns of mesothelioma should be present as well, which help facilitate the diagnosis. In addition, malignant mesotheliomas often show diffuse infiltration, increased cytological atypia with prominent nucleoli and increased mitotic activity, which are helpful clues to the diagnosis. Localised mesothelioma may be even more challenging to differentiate from adenomatoid tumours. Fortunately, these tumours are most often found within the pleura, contain cytological atypia and rarely show classic features of adenomatoid tumour. The identification of BAP1 loss can be helpful in confirming the diagnosis of mesothelioma. However, it should be emphasised that only a subset of mesotheliomas show loss of BAP1, and thus retained expression does not exclude the diagnosis.[40,41]

In summary, adenomatoid tumours involving the gastrointestinal tract and liver are uncommon and can mimic other tumours seen within the abdomen, such as adenocarcinoma and mesothelioma. Adenomatoid tumour should be kept in mind when the pathologist encounters an incidentally discovered, relatively well-circumscribed lesion composed of bland tubules without significant cytological atypia in a prominent, often fibrotic, stroma. Although follow-up is often limited in these patients, there have been no reported cases of tumour recurrence or metastasis,

and thus it is important to differentiate these tumours from malignant lesions that portend a much worse prognosis.

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Conflicts of interest

None of the authors have any conflicts or relationships to disclose.

References

1. Quigley JC, Hart WR. Adenomatoid tumors of the uterus. *Am. J. Clin. Pathol.* 1981; **76**; 627–635.
2. Karpathiou G, Hiroshima K, Peoc'h M. Adenomatoid tumor: a review of pathology with focus on unusual presentations and sites, histogenesis, differential diagnosis, and molecular and clinical aspects with a historic overview of its description. *Adv. Anat. Pathol.* 2020; **27**; 394–407.
3. Sangoi AR, McKenney JK, Schwartz EJ, Rouse RV, Longacre TA. Adenomatoid tumors of the female and male genital tracts: a clinicopathological and immunohistochemical study of 44 cases. *Mod. Pathol.* 2009; **22**; 1228–1235.
4. Isotalo PA, Keeney GL, Sebo TJ, Riehle DL, Cheville JC. Adenomatoid tumor of the adrenal gland: a clinicopathologic study of five cases and review of the literature. *Am. J. Surg. Pathol.* 2003; **27**; 969–977.
5. Natarajan S, Luthringer DJ, Fishbein MC. Adenomatoid tumor of the heart: report of a case. *Am. J. Surg. Pathol.* 1997; **21**; 1378–1380.
6. Kaplan MA, Tazelaar HD, Hayashi T, Schroer KR, Travis WD. Adenomatoid tumors of the pleura. *Am. J. Surg. Pathol.* 1996; **20**; 1219–1223.
7. Yeh CJ, Chuang WY, Chou HH, Jung SM, Hsueh S. Multiple extragenital adenomatoid tumors in the mesocolon and omentum. *APMIS* 2008; **116**; 1016–1019.
8. Isotalo PA, Nascimento AG, Trastek VF, Wold LE, Cheville JC. Extragenital adenomatoid tumor of a mediastinal lymph node. *Mayo Clin. Proc.* 2003; **78**; 350–354.
9. Golden A, Ash J. Adenomatoid tumors of the genital tract. *Am. J. Pathol.* 1945; **21**; 63–79.
10. Zhao M, Li C, Zheng J, Yan M, Sun K, Wang Z. Cystic lymphangioma-like adenomatoid tumor of the adrenal gland: report of a rare case and review of the literature. *Int. J. Clin. Exp. Pathol.* 2013; **6**; 943–950.
11. Raaf HN, Grant LD, Santoscoy C, Levin HS, Abdul-Karim FW. Adenomatoid tumor of the adrenal gland: a report of four new cases and a review of the literature. *Mod. Pathol.* 1996; **9**; 1046–1051.
12. Craig JR, Hart WR. Extragenital adenomatoid tumor: evidence for the mesothelial theory of origin. *Cancer* 1979; **43**; 1678–1681.
13. Ferenczy A, Fenoglio J, Richart RM. Observations on benign mesothelioma of the genital tract (adenomatoid tumor). *Cancer* 1972; **30**; 244–260.
14. Davy CL, Tang CK. Are all adenomatoid tumors adenomatoid mesotheliomas? *Hum. Pathol.* 1981; **12**; 360–369.
15. Mucientes F. Adenomatoid tumor of the epididymis: ultrastructural study of three cases. *Pathol. Res. Pract.* 1983; **176**; 258–268.
16. Taxy JB, Battifora H, Oyasu R. Adenomatoid tumors: a light microscopic, histochemical, and ultrastructural study. *Cancer* 1974; **34**; 306–316.
17. Delahunt B, Eble JN, King D, Bethwaite PB, Nacey JN, Thornton A. Immunohistochemical evidence for mesothelial origin of paratesticular adenomatoid tumour. *Histopathology* 2000; **36**; 109–115.
18. Wang W, Zhu H, Wang J *et al*. Clonality assessment of adenomatoid tumor supports its neoplastic nature. *Hum. Pathol.* 2016; **48**; 88–94.
19. Tamura D, Maeda D, Halimi SA *et al*. Adenomatoid tumour of the uterus is frequently associated with iatrogenic immunosuppression. *Histopathology* 2018; **73**; 1013–1022.
20. Goode B, Joseph NM, Stevers M *et al*. Adenomatoid tumors of the male and female genital tract are defined by TRAF7 mutations that drive aberrant NF-kB pathway activation. *Mod. Pathol.* 2018; **31**; 660–673.
21. Itami H, Fujii T, Nakai T *et al*. TRAF7 mutations and immunohistochemical study of uterine adenomatoid tumor compared with malignant mesothelioma. *Hum. Pathol.* 2021; **111**; 59–66.
22. Lao IW, Wang J. Adenomatoid tumor of the small intestine: the first case report and review of the literature. *Int. J. Surg. Pathol.* 2014; **22**; 727–730.
23. Hayes SJ, Clark P, Mathias R, Formela L, Vickers J, Armstrong GR. Multiple adenomatoid tumours in the liver and peritoneum. *J. Clin. Pathol.* 2007; **60**; 722–724.
24. Hanada S, Okumura Y, Kaida K. Multicentric adenomatoid tumors involving uterus, ovary, and appendix. *J. Obstet. Gynaecol. Res.* 2003; **29**; 234–238.
25. Nagata S, Aishima S, Fukuzawa K *et al*. Adenomatoid tumour of the liver. *J. Clin. Pathol.* 2008; **61**; 777–780.
26. Overstreet K, Wixom C, Shabaik A, Bouvet M, Herndier B. Adenomatoid tumor of the pancreas: a case report with comparison of histology and aspiration cytology. *Mod. Pathol.* 2003; **16**; 613–617.
27. Van Seventer I, Verheij J, Phoa S, Van Gulik TM. A cystic, septated lesion in the liver with unusual diagnosis. *BMJ Case Rep.* 2014. https://doi.org/10.1136/bcr-2014-207687
28. Adachi S, Yanagawa T, Furumoto A *et al*. Adenomatoid tumor of the liver. *Pathol. Int.* 2012; **62**; 153–154.
29. Hatano Y, Hirose Y, Matsunaga K *et al*. Combined adenomatoid tumor and well differentiated papillary mesothelioma of the omentum. *Pathol. Int.* 2011; **61**; 681–685.
30. Skafida E, Tsavari A, Koulia K *et al*. Extragenital adenomatoid tumour of the omentum: an unusual location. *OA Case Rep.* 2013; **2**; 4.
31. Ruiz-Tovar J, Santos J, Lopez-Delgado A, Orduña A, Calpena R. Transmural peritoneal adenomatoid tumour in the ileocaecal region causing massive haemoperitoneum and low gastrointestinal bleeding: differential diagnosis with capillary haemangiomas. *Ann. R. Coll. Surg. Engl.* 2011; **93**; e3–e5.

32. Grosse-Holz M, Streitberg UV, Thies J, Lenhart M, Seitz G. Cystic tumor on the porta hepatis. *Pathologe* 2013; **34**; 463–465.
33. Hanrahan JB. A combined papillary mesothelioma and adenomatoid tumor of the omentum. Report of a Case. *Cancer* 1963; **16**; 1497–1500.
34. Stevers M, Rabban JT, Garg K *et al*. Well-differentiated papillary mesothelioma of the peritoneum is genetically defined by mutually exclusive mutations in TRAF7 and CDC42. *Mod. Pathol.* 2019; **32**; 88–99.
35. Livingston EG, Guis MS, Pearl ML, Stern JL, Brescia RJ. Diffuse adenomatoid tumor of the uterus with a serosal papillary cystic component. *Int. J. Gynecol. Pathol.* 1992; **11**; 288–292.
36. Phitayakorn R, MacLennan G, Sadow P, Wilhelm S. Adrenal adenomatoid tumor in a patient with human immunodeficiency virus. *Rare Tumors* 2011; **4**; e21.
37. Piccin A, Conneallly E, Lynch M, McMenamin ME, Langabeer S, McCann S. Adenomatoid tumor of the testis in a patient on imatinib therapy for chronic myeloid leukemia. *Leuk. Lymph.* 2006; **47**; 1394–1396.
38. Angeles-Angeles A, Reyes E, Muñoz-Fernandez L, Angritt P. Adenomatoid tumor of the right adrenal gland in a patient with AIDS. *Endocr. Pathol.* 1997; **8**; 59–64.
39. Mizutani T, Yamamuro O, Kato N *et al*. Renal transplantation-related risk factors for the development of uterine adenomatoid tumors. *Gynecol. Oncol. Rep.* 2016; **17**; 96–98.
40. Karpathiou G, Peoc'h M. Pleura revisited: from histology and pathophysiology to pathology and molecular biology. *Clin. Respir. J.* 2019; **13**; 3–13.
41. Hung YP, Dong F, Dubuc AM *et al*. Molecular characterization of localized pleural mesothelioma. *Mod. Pathol.* 2020; **33**; 271–280.