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Review

Pseudomyxoma peritonei

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Background Pseudomyxoma peritonei is an unusual condition in which gelatinous fluid collections are associated with mucinous implants on the peritoneal surfaces and omentum. The pathological origin and ideal treatment of the condition are subjects of debate.

Methods An unrestricted Medline search over 1986–1997 was performed for pseudomyxoma peritonei.

Results and conclusions There is increasing evidence that pseudomyxoma peritonei is a neoplastic condition which usually arises from a primary adenoma or adenocarcinoma of the appendix. Reported series include a spectrum of pathological lesions, from entirely benign ruptured mucocele to advanced carcinoma. This, and the rarity of the condition, limit the conclusions that can be drawn regarding its treatment and prognosis. Most authorities agree that a thorough surgical debulking should be made. In most cases this will be a difficult and time-consuming undertaking, possibly requiring cooperation between two or more specialists and consideration of delivering intraperitoneal adjuvant therapy during or immediately after surgery. Treatment therefore requires a planned approach with accurate preoperative assessment of the diagnosis and the extent of the condition. There is some largely anecdotal evidence in favour of intraperitoneal chemotherapy and radioisotope treatment. Ultraradical surgery, with heated intraoperative and further postoperative chemotherapy, is strongly advocated by one group but remains contentious. The majority of patients will eventually suffer recurrence. The 5-year survival rate ranges from 53 to 75 per cent, but outcomes vary widely between relatively benign and malignant subgroups.

Pseudomyxoma peritonei is an unusual condition in which diffuse collections of gelatinous fluid are associated with mucinous implants on the peritoneal surfaces and omentum. It is two to three times more common in females than males and is said to be present in two of every 10 000 laparotomies[1]; it is often an unexpected finding. The term 'jelly belly'[2] has been used to characterize the large accumulations of mucinous ascites that may be encountered at laparotomy.

A clinical case consistent with this diagnosis was first described by Rokitansky in 1842[3], but it was Werth[4] who first coined the term pseudomyxoma peritonei in 1884 when he described its occurrence in association with a mucinous carcinoma of the ovary. The term *pseudo*-myxoma referred to chemical differences from other types of mucin that had been analysed. In 1901 Frankel[5] described it in association with a cyst of the appendix.

After these early descriptions, a debate arose about the significance of ovarian and appendiceal disease as the origin of pseudomyxoma peritonei. Simultaneous disease is found at these two sites in the vast majority of female patients with this condition. Recent applications of immunocytochemistry and genetic analysis by the polymerase chain reaction have made a major contribution to the resolution of this debate.

Pathological origin

The study of pseudomyxoma peritonei is limited by the rarity of the condition and the small number of cases collected in published series. Most of these series are retrospective and use differing inclusion criteria. They may be biased towards different types of disease process by presentation to surgical or gynaecological units.

Many gynaecological publications have emphasized the association with ovarian mucinous tumour of low malignant potential (MLMP), also termed mucinous borderline tumour. Standard textbooks have often simply accepted that any mucinous ovarian tumour present in a female represents the origin of the disease[6,7]. However, when the appendix is examined histologically, mucoceles, adenomas or carcinomas are found in nearly all cases. This simultaneous disease in most female patients might be explained either on the basis of spread from the appendix to the ovary or on the basis of two independent primary disease processes. If there is a single primary neoplasm other deposits should show features consistent with a clonal origin. If there is more than one primary neoplastic lesion a predisposing field change is implied. It has been suggested that this might arise because of mucinous metaplasia due to chronic irritation from ascitic fluid[8,9].

Many reports describe pseudomyoxoma peritonei in association with a ruptured mucocele of the appendix and do not mention neoplasia. Cheng[10] successfully reproduced mucoceles of the appendix by ligating the organ in rabbits, but subsequent sterile rupture of the mucoceles did not lead to pseudomyxoma peritonei. Carr *et al.*[11] have made an extensive clinicopathological study of tumours and tumour-like lesions of the appendix. In their 11 cases of simple mucocele, dissection of the wall by acellular mucin was frequently observed and three patients formed a localized collection of acellular mucin in the right lower

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quadrant. However, pseudomyxoma peritonei did not develop. It is now generally accepted that pseudomyxoma peritonei is due to neoplastic mucus-secreting cells within the peritoneal cavity. These cells may have low-grade cytological appearances and be sparsely distributed within collections of extracellular mucin, but they will invariably be identified when appropriate techniques are applied[12]. Carr[13] believes, because of the relentless growth of the cells, that pseudomyxoma peritonei should always be classed as a malignant condition irrespective of other histological features. However, there is no consensus of opinion on this matter. Nor is there agreement as to a point of separation between pseudomyxoma peritonei and carcinomatosis peritonei due to advanced, high-grade, mucinous carcinomas, which may also produce extracellular mucin within the peritoneal cavity.

Certain features of pseudomyxoma peritonei tend to support the hypothesis that most cases originate in the appendix with frequent secondary spread to the ovary. Proponents of this hypothesis point out that the ovarian tumours are either bilateral or else predominantly right-sided; only 20 per cent occur on the left side alone[14]. The histological appearances often suggest implantation of tumour on the surface of the ovary. Pseudomyxoma ovarii is the name given to the histological appearance of mucin dissecting through the stroma of the ovary. It is considered to be a feature of secondary ovarian tumours and is seen in 88 per cent of cases of pseudomyxoma peritonei but in only 25 per cent of uncomplicated ovarian MLMPs[15]. It is also pointed out that the appendix and ovary are unlikely to share a common predisposition to neoplasia when they have different embryological origins. Except in pseudomyxoma peritonei, it is extremely rare for appendiceal and ovarian neoplasms to occur simultaneously.

Those who believe that the ovarian disease is usually a primary process argue that the low histological grade of the ovarian lesions would be surprising for a metastasizing neoplasm. They also point to the fact that metastases to other solid organs are extremely rare in pseudomyxoma peritonei.

In 1993 Seidman *et al.*[15] argued strongly that pseudomyxoma peritonei represents 'multifocal neoplasia of the peritoneum, ovary and appendix'. They supported this view with a study of 15 cases of pseudomyxoma peritonei with ovarian and appendiceal disease. Specimens from both sites were tested with four immunoperoxidase stains. One representative block each from the ovarian tumour and the appendiceal tumour were evaluated, together with a representative block from a deposit in the omentum or peritoneum. Concordance of staining was demonstrated in only five of 15 cases. Kahn *et al.*[16] and Kaern *et al.*[17] also favoured the concept of multiple primary tumours arising because of a field change in the tissues concerned. They drew similar conclusions from clinical and histological data. However, Young *et al.*[14] criticized Seidman's conclusions, noting that heterogeneity of immunohistochemical staining is not uncommon within the same tumour. One of their own studies[18] analysed clinical and histological features in 22 cases of pseudomyxoma peritonei with both appendiceal and ovarian disease; they concluded that the ovarian tumours were probably secondary to primary appendiceal lesions. Prayson *et al.*[19] reached the same conclusion from analysis of 17 similar cases.

Ronnett *et al.*[20] defined criteria for the diagnosis of secondary ovarian involvement and found that these were satisfied in 28 of 30 cases of pseudomyxoma peritonei. No case of unequivocal ovarian origin was identified. Recent immunohistochemical findings have added strong support to the theory that most, if not all, tumours associated with pseudomyxoma peritonei originate from a primary in the appendix. Ronnett *et al.*[21] performed a study based on the fact that nearly all ovarian MLMPs and mucinous carcinomas stain positively for cytokeratin (CK) 7, 18 and 20, as well as carcinoembryonic antigen (CEA) and human alveolar macrophage (HAM) 56; most colorectal adenocarcinomas are positive for CK 20 and CEA but negative for CK 7 and HAM-56. In 13 cases of pseudomyxoma peritonei, appendiceal mucinous adenomas and ovarian tumours from the same patient were stained for these antigens. In ten of 13 cases the staining patterns were identical at the two separate sites. In eight of these cases a typical 'colorectal' pattern of staining was demonstrated. In two of the remaining patients with identical staining patterns at the two sites, the pattern was 'colorectal' except for a positive CK 7. The typical colorectal pattern was also seen in the ovary of an additional case with no appendiceal specimen. A control group of ovarian MLMP tumours was then analysed. The frequency of immunopositivity for CK 7 and HAM-56 was significantly different between the two groups, with the ovarian tumours in pseudomyxoma peritonei tending to be negative for CK 7 and HAM-56, and so similar to the appendiceal tumours. This was in marked contrast to the findings from the control group of ovarian MLMP tumours. These authors concluded that most ovarian tumours in pseudomyxoma peritonei are immunophenotypically identical to associated appendiceal tumours and distinct from primary MLMPs. Two smaller cytokeratin studies[22,23] were inconclusive but not inconsistent with this conclusion. Cuatrecasas *et al.*[24] used the polymerase chain reaction to study c-*Ki-ras* mutations in ovarian and appendiceal tumours from patients with pseudomyxoma peritonei. Identical mutations were present at the two sites in all six cases studied.

A dissenting voice has, however, been sounded by Chuaqui *et al.*[25], who found some heterogeneity in genetic microsatellites from similarly paired specimens. These authors concluded that second primary tumours were present in some cases.

In addition to discussion of pseudomyxoma peritonei in association with appendiceal and ovarian tumours, the literature also contains sporadic case reports of associations with tumours of the colon and rectum[26], lung[27], breast[28], pancreas[29], stomach[26,30], gallbladder and bile ducts[31], fallopian tubes[32,33] small intesine and urinary bladder[26]. Another report has attributed the disease to retained rectal tissue after proctectomy[2].

Both case reports and collected series of pseudomyxoma peritonei represent a heterogenous group of pathological lesions. Ronnett *et al.*[12] suggested that some may have little in common other than the production of abundant extracellular mucin. Because of the considerable variation in applying different pathological terms, they proposed that pseudomyxoma peritonei be defined as 'a clinicopathological entity characterized by mucinous ascites and non-invasive mucinous implants with a characteristic distribution and containing histologically benign mucinous epithelium derived from an appendiceal mucinous adenoma and having a benign clinical course'. Cases fitting this definition were to be labelled as having 'disseminated peritoneal adenomucinosis', whereas similar cases, but with malignant histological features, were to be

classified as 'peritoneal mucinous carcinomatosis'. In their painstaking study of 109 patients they also required an intermediate group for 14 cases that could not be allocated satisfactorily to either of these categories. Helpful as these definitions are, no other groups have yet adopted them in published studies of pseudomyxoma peritonei.

Clinical presentation and investigation

In series published to date, pseudomyxoma peritonei has usually been an unexpected diagnosis made at laparotomy. The preoperative diagnosis has often been one of appendicitis or an ovarian tumour. The most commonly recorded symptoms have been abdominal pain, distension or a mass in the abdomen. Nausea, vomiting, fatigue and urinary symptoms have also been described[20,34], as well as presentation with a scrotal mass[35]. In one series[36] more than 25 per cent of patients presented with the finding of mucinous tumour in the sac of a hernia.

At operation, a variable volume of mucinous ascites has been found, together with tumour deposits that typically involve the right hemidiaphragm, the right retrohepatic space, the left paracolic gutter and the ligament of Treitz. The peritoneal surfaces of the bowel are usually free of tumour[37]. The appendix is usually abnormal and one or both ovaries may be involved. The formation of bulky secondary disease from a small primary has been termed a 'redistribution phenomenon'[37]. The sites of predilection may reflect mucin production, absence of adhesion molecules on the pseudomyxoma cells, peristalsis of the intestines, gravity and the presence of open lymphatic lacunae on the omentum and undersurface of the diaphragm[37].

Imaging

Many reports refer to cases discovered before ultrasonography, computed tomography (CT) or magnetic resonance imaging (MRI) were used regularly in the investigation of abdominal complaints. Most other articles on imaging in pseudomyxoma peritonei are based on reports of three or four cases. Many such reports continue to be quoted years after publication to validate statements on the findings of imaging in this condition[38–41]. The sensitivity and specificity of these findings have never been assessed objectively and are never likely to be because of the rarity of the condition. The most substantial account of imaging in pseudomyxoma peritonei comes from Walensky *et al.*[42] who described 33 patients from the Johns Hopkins Hospital in Baltimore, Maryland, USA, who had at least one of the following studies: plain radiography, barium studies, ultrasonography, CT or MRI. Regrettably, the numbers assessed by each modality are not stated for the last three modalities.

Imaging before surgery is highly desirable, as a preoperative diagnosis allows the operation to be planned and performed by a surgeon with the necessary time, facilities and skills to carry out radical debulking and institute intraperitoneal adjuvant treatment, where appropriate. It is also valuable in the assessment of recurrent disease.

Plain radiography and contrast studies. Plain films are generally considered unhelpful for diagnosis but may show central displacement of the intestines and obliteration of the psoas shadows[42,43]. Rarely, punctate, annular or curvilinear calcifications are seen within the gelatinous masses in pseudomyxoma peritonei[44].

Radiography with contrast media was performed in 21 cases in the Baltimore series[42] and in new cases invariably demonstrated the lack of bowel lumen involvement that is characteristic of the relatively non-invasive deposits found in pseudomyxoma peritonei. Barium enema also served to exclude colorectal tumours and to assess large bowel obstruction, particularly in recurrent disease.

Ultrasonography. Ultrasonography is frequently employed and typically shows non-mobile echogenic ascites with 'scalloping' of the hepatic and splenic margins due to extrinsic pressure of adjacent peritoneal implants[41,42]. The echogenic texture may be interspersed with areas of hypoechogenicity. The echogenicity of the ascites corresponds with semisolid gelatinous masses and the walls of tiny mucinous cysts[40]. Early experience with endoscopic ultrasonography has also been reported[45].

Computed tomography. CT is now widely employed to establish the diagnosis and extent of pseudomyxoma peritonei[42]. The mucinous material is similar in density to fat and appears heterogeneous[2]. Scalloping of the liver, spleen and mesentery are easily demonstrated together with central displacement of bowel loops. The occasional calcifications mentioned in connection with plain radiography are also seen on CT. Sugarbaker *et al.*[36] use two features of the CT scan to make a preoperative distinction between peritoneal adenomucinosis and peritoneal mucinous carcinomatosis. The presence of tumour greater than 5 cm on the jejunum, proximal ileum or adjacent mesentery is said to indicate either a mucinous adenocarcinoma or impaction of adenomucinosis within the abdomen and pelvis. Focal narrowing of small bowel loops with segmental obstruction indicates peritoneal adenocarcinomatosis. None the less, Hameed *et al.*[46] wrote a cautionary case report of a patient with endometriosis who was wrongly suspected of having pseudomyxoma peritonei despite CT.

Magnetic resonance imaging. There are even fewer data on MRI, the application of which is limited by expense and poor availability of equipment. The authors from Baltimore[42] failed to mention how many MRI scans were performed on their patients. The same morphological features seen on CT can be demonstrated on MRI. Buy *et al.*[39] have reported that T2-weighted images provide optimal contrast from normal tissue. They also stated that MRI may be particularly sensitive for the detection of visceral invasion but their conclusions are based on the study of three cases.

Cytology and frozen-section histology

A number of authors have studied the cytological appearances of peritoneal aspirates from patients with pseudomyxoma peritonei[47–52]. Between two and nine patients form the basis of these reports. Direct smears and smears from centrifuged or filtered material were used. These authors agree that the aspirates typically contain much mucus and few cells. The mucus stains positively with periodic acid–Schiff, astra blue, mucicarmine and alcian blue. The mucin is typically clumped in a network of slender, benign-looking cells

which have the appearance of fibroblasts. In the marginal areas of the clumps and around them, plump, rounded 'mesothelial' cells are seen. Malignant cells are not frequently noted and will not necessarily be identified even when a histological diagnosis of carcinoma is subsequently made. Typical appearances were not identified in all of the cases reported and, in some, they could be identified only after retrospective review of the cytological material. From these reports, it is impossible to assess the sensitivity and specificity of aspiration cytology in the diagnosis of pseudomyxoma peritonei. Hence, its value in clinical practice remains uncertain.

Frozen section has sometimes been employed for rapid histological assessment of operative biopsies. However, this method may make it particularly difficult to separate the microscopic appearances from those of endometriosis[53].

Tumour markers

Zoetmulder and Sugarbaker[54] advocate the measurement of CEA levels but do not report any data on levels in their patients. A few authors have retrospectively reported the levels of CEA and CA19-9 in very small numbers of patients[47,55]. These anecdotal data indicate only that levels of CEA and, perhaps CA19-9, are not infrequently raised in patients with pseudomyxoma peritonei and may rise in association with recurrent disease. In a report of four patients with pseudomyxoma peritonei and mucinous ovarian tumours, three also had a raised CA125 level[56].

Treatment

No active treatment

Friedland *et al.*[57] argued that active treatment was not necessarily desirable in pseudomyxoma peritonei. Their paper described a single patient whose abdominal distension was believed to have increased asymptomatically for 5 years before diagnosis. No follow-up after diagnosis was mentioned. They asserted that patients with pseudomyxoma peritonei survive for many years with few problems. However, the only supporting evidence cited is an old textbook and an article[58] that actually describes survival after radical surgery.

Surgery

Thorough surgical debulking is widely regarded as the mainstay of treatment in this condition[19,34,59–61]. As far as possible, all gross disease should be removed. The appendix should also be removed for histological assessment.

Ultra-radical surgery and adjuvant treatment. Sugarbaker, who has published extensively on pseudomyxoma peritonei, advocates a particularly rigorous surgical approach which involves systematic excision of affected peritoneal surfaces with diathermy. He has published a clear and well illustrated account of the relevant techniques[62], which in certain sectors of the abdomen involve routine excision of the gastric antrum, rectosigmoid colon or gallbladder. In addition, a right hemicolectomy is frequently performed. Using these techniques with adjuvant intraperitoneal and systemic chemotherapy, Sugarbaker *et al.*[63] claimed excellent results in a series of patients with pseudomyxoma peritonei. However, for the reasons discussed above, it is impossible to be certain that these patients are fully comparable with those in other series. Gough *et al.*[34] have drawn attention to the high complication rate and short follow-up in the published data of Sugarbaker and co-workers.

More recently Sugarbaker *et al.*[36] have published an updated account of their series, which now includes at least 131 patients; an exact figure cannot be quoted because of inconsistencies within the tabulated data in that report. The separation of patients into groups with adenomucinosis, mucinous carcinoma and intermediates allows them to highlight an excellent 5-year survival rate of 80 per cent in their best pathological group, but the present authors calculate that the overall 5-year survival rate for all pathological categories is only 60 per cent, which is barely better than the historical figures from the Mayo Clinic reported by Gough *et al.*[34]. This being the case, it is particularly unfortunate that Gough *et al.*'s median survival and 5-year survival rates are substantially misquoted in their paper[36]. The paper discusses operative morbidity and mortality for 138 patients whose peritonectomy operations took a mean of 11 h and involved a mean blood loss of 1700 ml and a mean of 2·5 intestinal anastomoses. The overall mortality rate was 2·7 per cent but no timescale was defined. This rate rose to 5 per cent with their most recent practice of giving intraoperative intraperitoneal chemotherapy heated to 44°C, but the difference was not statistically significant. The overall complication rate was 36·1 per cent. Nine per cent of patients had pulmonary complications that were not described in any more detail; all other complications were major. The mean duration of ileus was 19·3 days. While Sugarbaker and co-workers are to be respected for their commitment to treating this disease and for their unique prospective collection of data on the condition, it is impossible to be sure that the complexity and complications of their techniques are justified. There is no valid control group with which their results can be compared. They attract many patients by tertiary referral whose prognosis may be better or, indeed, worse than those presenting to other centres.

Mucolytic agents

Green *et al.*[64] were the first to advocate the use of dextrose solution to loosen the mucinous deposits. Other authors have been enthusiastic about the use of this and other suggested mucolytic substances[65,66], both as an aid to operative cytoreduction and as a means of obtaining closed catheter drainage of mucinous material for palliation. However, a laboratory study[67] failed to demonstrate any mucolytic advantage of 5 per cent dextrose and some other solutions when compared with normal saline. Furthermore, a recent report[68] described an incident of potentially fatal hyperglycaemia due to the use of dextrose for peritoneal lavage.

Phototherapy

Sindelar *et al.*[69] have produced a detailed technical description of the use of photosensitizers and laser light as an adjuvant to conventional dissection at laparotomy for disseminated peritoneal malignancy, including

pseudomyxoma peritonei. Unfortunately, the article does not begin to address the question of its efficacy as a treatment for pseudomyxoma peritonei. As with hyperthermia (see below), phototherapy suffers from obvious technical difficulties, potential complications and lack of proven clinical benefit.

Chemotherapy and intraperitoneal hyperthermic chemotherapy

While some authors are enthusiastic about the results they have obtained with adjuvant chemotherapy[36,70], reports are essentially anecdotal. No formal trials have been conducted, even against historical controls. Therefore, there are no hard data to establish the benefits of adjuvant chemotherapy in this condition.

Many agents have been tried either as systemic treatment or as intraperitoneal infusions during or after surgery. The most widely used have been 5-fluorouracil (5-FU), cyclophosphamide and mitomycin C for intraperitoneal treatment, and 5-FU, cyclophosphamide, L-phenylalanine mustard and doxyrubicin for systemic treatment. Cisplatinum, which is known to be effective in ovarian cancer, has been used by both intraperitoneal and systemic routes. Interestingly, it is not clearly beneficial in pseudomyxoma peritonei[1].

In the Mayo Clinic series[34], retrospective review showed that survival was significantly more likely in patients given intraperitoneal chemotherapy and less likely in those given systemic chemotherapy. However, this result might have been due entirely to selection bias. In the series from the Memorial Sloan-Kettering Cancer Center[71] there was no significant difference in survival between similarly compared groups given and not given chemotherapy.

Most recent work has focused on intraperitoneal delivery of chemotherapy, with particular interest in the use of solutions heated to temperatures of around 44°C. The theoretical benefits of such treatment for peritoneal carcinomatosis from appendiceal and colorectal cancer have been well elaborated by Sugarbaker[72]. The pharmacokinetics of intraperitoneal chemotherapy indicate that high concentrations of agents such as 5-FU and mitomycin C can be delivered to peritoneal tumour deposits without producing toxic systemic levels[73,74]. Penetration is particularly effective in superficial tumour deposits that have not invaded deeply from the peritoneal surface. Pseudomyxoma peritonei should, in theory, be ideally suited to this treatment, particularly as bloodborne and lymphatic metastases are uncommon in this condition. Interest in using hyperthermic solutions arises from *in vitro* studies indicating that they may be more cytotoxic to tumour cells than solutions at body temperature[75–77].

There is some direct evidence that intraperitoneal chemotherapy produces improvement in the histological appearance of residual deposits of disseminated colorectal and appendiceal carcinoma resampled at a second laparotomy[78]. Changes are distributed patchily throughout the abdomen, presumably due to the difficulty of delivering an even application of the treatment. This has led one exponent of the technique to change from giving intraperitoneal chemotherapy solely in the postoperative period to starting it during operation, when it can be manually swilled around the peritoneal cavity, albeit with a somewhat demanding technique to avoid spillage[36]. The results for various peritoneal tumours treated by Sugarbaker's group[79] and work on gastric cancer from Japan[76] indicate that adjuvant intraperitoneal chemotherapy is associated with a better outcome if a complete surgical cytoreduction has been achieved.

While conclusive evidence for the use of adjuvant chemotherapy may be difficult or impossible to obtain in a rare condition such as pseudomyxoma peritonei, its further study will be encouraged by the results of a limited trial of adjuvant hyperthermic chemotherapy in peritoneal carcinomatosis secondary to gastric cancer[80]. This showed a significant survival advantage for patients so treated, 31 per cent of whom survived for 5 years.

Radiotherapy

The Mayo Clinic series[34] produced a survival advantage for patients treated with intraperitoneal radioisotopes, but, as mentioned above, this was only a retrospective comparison of non-randomized groups. The isotopes ^{32}P and ^{198}Au have been used in this context. External-beam radiotherapy has been used in the past for primary adjuvant treatment and for recurrences[81–83], but has obvious drawbacks in the abdomen and is associated with substantial morbidity. Early experience with radioimmunotherapy for solid cancers has been reviewed by Kairemo[84], who reported a few cases of pseudomyxoma peritonei treated in this way in his department.

Treatment of recurrent disease

At the benign end of the disease spectrum, pseudomyxoma peritonei is a disease that progresses slowly and in which recurrences may take years to develop or become symptomatic. Jahne *et al.*[85] have described a low rate of perioperative morbidity, even after multiple relaparotomies, and therefore argue for surgical treatment of recurrent disease. Surgery for recurrent pseudomyxoma peritonei is usually difficult because of adhesions and fibrosis, greatly increasing the risk of unintentional enterotomies and subsequent leaks and fistulas. However, it is widely accepted that recurrences should be investigated vigorously and treated with further surgical debulking, with or without adjuvant chemotherapy, in the expectation that many patients will enjoy substantial additional survival and freedom from symptoms.

Outcome

The study of mortality and disease recurrence in pseudomyxoma peritonei is confounded by the small number of patients collected with adequate follow-up data, and the fact that different series have different inclusion criteria that may bias their populations towards more or less aggressive extremes of the disease.

Recurrence

The median follow-up period of 12 (range 9–25·6) years for surviving patients in the Mayo Clinic series[34] is considerably better than in most other reports of pseudomyxoma peritonei. Seventy-six per cent of patients ultimately developed recurrence and 50 per cent of recurrences occurred within 2·5 years. If the debulking procedure excised all viable tumour, symptomatic recurrence occurred later than after a subtotal debulking

(mean 2·6 *versus* 1·9 years). Of the 38 patients requiring a second operation because of recurrence, 24 went on to a third operation and 15 to a fourth procedure. The timescale of the further recurrences and the lengths of survival after recurrence is, unfortunately, not clear from this paper. At the Massachusetts General and Brigham and Women's Hospitals[60], the total recurrence rate was 52 per cent in 23 patients, but a shorter period of follow-up was reported. Sugarbaker *et al.*[36] reported that approximately one-third of their patients required reoperation for recurrent adenomucinosis. This was presumably the recurrence rate in their best prognostic group of patients with disseminated peritoneal adenomucinosis.

Complications

Primary pseudomyxoma peritonei usually causes little interference with the function of the abdominal organs even when there is considerable bulk of disease. As with other pelvic tumours, obstruction of venous return from the lower limbs has been reported[83], as has ureteric obstruction[86]. Recurrent disease is much more likely to occur on the bowel surfaces[54] and is regularly associated with intense fibrosis and adhesions. For this reason, intestinal obstruction and obstructive jaundice are common and are often a cause of death in pseudomyxoma peritonei. Metastases to lymph nodes and to the parenchyma of solid organs are unusual and nearly always represent disease due to a relatively high-grade mucinous carcinoma.

Survival

Median survival of 5·9 years, and 5- and 10-year survival rates of 53 and 32 per cent respectively were reported for 56 patients collected between 1957 and 1983 at the Mayo Clinic[34]; equivalent figures for 17 cases of pseudomyxoma peritonei 'of appendix origin' at the Memorial Sloan-Kettering Cancer Center were 6·25 years, 75 and 10 per cent[71]. If the disease is subclassified it becomes clear that survival is considerably worse in patients with more malignant clinical and histological features. When Ronnett and colleagues[12] subdivided their cases into 'disseminated peritoneal adenomucinosis' and 'peritoneal mucinous carcinomatosis' they were able to report a 5-year survival rate of 84 per cent in the former and 6·7 per cent in the latter group, with 33·6 per cent in an intermediate group. Similarly, workers at Sacramento have reported a 3-year survival rate of 80 and 4 per cent respectively for patients with non-invasive and invasive deposits[26].

Conclusions

Recent applications of immunocytochemistry and studies of genetic material using the polymerase chain reaction have increased the likelihood that most cases of pseudomyxoma peritonei are due to metastases from neoplasms of the appendix. Because of the rarity and heterogeneity of the condition, there is little hard evidence regarding optimum treatment, but expert opinion favours radical surgical debulking with or without adjuvant intraperitoneal chemotherapy or radioisotope treatment. The majority of patients develop recurrent disease at widely varying intervals after the original diagnosis. Further debulking is then indicated, but this is likely to be difficult owing to fibrosis, adhesions and possible intestinal obstruction. Five-year survival rates of 50–70 per cent are to be expected.

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