SPONTANEOUS INTESTINAL PERFORATION

ANNA PIOTROWSKA, BARBARA ANTONIAK, ANDRZEJ KAMIŃSKI

Department of Pediatric Surgery, Warsaw Medical University
Kierownik: prof. dr hab. A. Kamiński

Spontaneous intestinal perforation (SIP) and necrotizing enterocolitis (NEC) are the reason of intestinal damage in preterm neonates with low and extremely low body weight. Etiology of SIP is still unknown. It has not been determined whether SIP is a separate disease entity or only benign form of necrotizing enterocolitis (NEC). Surgical treatment includes peritoneal drainage, resection and primary intestinal anastomosis or temporary ileostomy.

The aim of the study was to estimate risk factors and the strategy of surgical treatment in SIP.

Material and methods. Between 2006 and 2008 ten patients undergone surgery for SIP. Retrospective analysis of patients’ data was performed.

Results. Mean gestational age was 26.1±3,143 Hbd, mean body weight 892±113.3 g. Sudden deterioration in the general condition with distension and lividity of the abdomen was correlated with radiological findings of perforation in all patients. Peritoneal drainage was performed in one patient, in one patient primary anastomosis was performed and multistages surgical treatment was done in the remaining. In resected segments of the intestine the histological signs of SIP were present. Two patients died, the follow-up of the remaining was maintaining for 4-24 months.

Conclusions. Definitive differentiation between SIP and NEC can be made only by intraoperative view and histological evaluation of resected intestine. Survival rate (80%) in the study group was correlated with individual surgical strategy and advances in neonatal care.

Key words: preterm neonate, spontaneous intestinal perforation, necrotizing enterocolitis

Spontaneous intestinal perforation (SIP) is one of the most common complication of the neonatal period (1). In 1988 Aschner described SIP as separate disease entity and Gordon defined its characteristic histological signs (2, 3).

Prevalence of SIP in neonates with body weight lower than 1500 g treated in the intensive care units ranged from 1.1 to 7.4% (4). Increasing prevalence of SIP is related most probably to the increased survival of preterm neonates with low and extremely low body weight (3, 5).

Etiology of SIP is still not known (4, 6, 7). Important role in intestinal damage is related to focal ischemia, motility impairment and hypoplasia of intestine muscle layer observed in the histological assessment (4, 6, 7, 8). Risk factors are the following: prematurity, low body weight, male sex, multiple pregnancy, respiratory distress. These factors along with the organ immaturity of the neonate can lead to the focal ischemia of the intestinal wall. Umbilical vessels catheterization and therapy with Indomethacine used in profylaxis of hemorrhage to the central nervous system or as a treatment of persistent ductus arteriosus can be the reasons, among other, of intestinal ischemia (4, 5, 7, 9, 10, 11).

Intestinal perforation is observed most commonly in the two first weeks of life of neonates with ventilatory support treatment and no enteral feeding. Sudden deterioration of the neonate general condition with the distention and lividity of the abdominal wall, biliary vomiting or retention in gastric tube correlates with the radiological signs of perforation. The most common finding on the abdominal radiological image is the presence of free air in the peritoneum (pneumoperitoneum). Airless ab-
demon with free fluid detected in the ultrasound examination can also indicate perforation. Radiological images differentiate perforation caused by necrotizing enterocolitis (NEC) only in the presence of gas vesicles in confluent of portal vein or in the intestinal wall (12, 13).

The results of the laboratory tests in the assessment of the advancement of the inflammatory process are similar in SIP and NEC (7, 13, 14). Initial levels of cytokines e.g. IL-8, IL-10 or I–FABP in the different stages of NEC are the promising way for monitoring the intestine damage level and possibly earlier differentiation between SIP and NEC (15-18).

The most common organisms cultured from blood and peritoneal fluid are Staphylococcus sp. In comparison to NEC other bacterial or fungal infections are identified less common. Bacteriological cultures are negative in 30% to 70% of cases (4, 12).

Recognition or suspicion of intestinal perforation is the indication for surgical treatment. Peritoneal drainage is an effective and definitive treatment option in approximately 40% of patients. But more frequently it is only the initial procedure before delayed laparotomy (1, 12, 13).

The most common localization of the perforation is a terminal part of ileum. Single or rarely multiple perforations 2-15 mm in diameter localized on the antimesentery edge of the terminal part of ileum are seen intraoperatively. The remaining segments of intestine are macroscopically unchanged (4, 7, 13). Most common multistage technique of the resection of involved part of intestine with the exposure of terminal fistulas and restoration of the continuity of the digestive system 3-6 months later is used (6, 13). Single publications indicate for effectiveness of the drainage with drain T through the perforation site (19). Resection and primary anastomosis is performed rarely (7, 13).

Characteristic microscopic findings in SIP are the following: haemorrhagic necrosis, lymphocyte infiltrations and muscle layer defect (4, 6, 7). Coagulation necrosis, extensive granulocyte infiltrations and the process of granulation tissue growth are typical for NEC (13).

Postoperative complications include general disturbances caused by secondary infection or arisen from intestinal motility and function (7, 13). Coincidence of intracranial haemorrhage, respiratory complications and congenital heart disease are also markedly important (3). The occurrence of the re-perforations even more than 30 days after first perforation was noted (5).

Survival of preterm neonates with SIP is almost twice than with NEC and range 70-100% (12, 20). Neonates with SIP have more favorable prognosis for psychomotor development (3, 21).

**MATERIAL AND METHODS**

10 preterm neonates treated surgically for spontaneous intestinal perforation between 2006-2008 were included into the study. The retrospective analysis of patients’ data was performed. The study group consists of 8 boys and 2 girls. Gestational age ranged from 23 Hbd to 33 Hbd (mean 26,1±3,143 Hbd). Gestational age in 9 of 10 patients was less than 30 Hbd. Five neonates were born by cesarean section, including delivery of triplets. Birth weights at birth ranged from 520 g to 1600 g (mean 892±113,3 g). Birth weights of 8 patients were lower than 1000 g. Apgar score in three patients was 1 and 3 in the 1st and 5th minute respectively. Two patients had 10 and 10 points in Apgar score in the 1st and 5th minute respectively. None of preterm infants had congenital abnormalities. In one patient intraventricular haemorrhage was detected in ultrasound examination.

In 8 patients mechanical ventilation was initiated immediately after birth because of respiratory insufficiency, in one patient respiratory support with the use of Infant-flow and one patient did not require any respiratory support. Therapy with Surfactant was performed in 7 of 10 patients. All patients received antibiotics – most often Ampicilline and Netromycine – due to the suspicion of intrauterine infection. Umbilical vessels were cannulated in 8 patients, of which in 7 umbilical vein and in 2 both vessels, vein and artery. Time of vessel catheter maintenance ranged from 3 till 8 days. Ibuprofen therapy due to persistent ductus arteriosus was used in 5 patients.

In one patient surgical closure of PDA had been performed before SIP occurrence. Trophic feeding was performed in 5 neonates. Five patients excreted meconium.
Analise of radiological images, bacteriological and histological data and surgical treatment was performed. Efficacy of different forms of surgical treatment was estimated.

**RESULTS**

All neonates were treated in NICU for 3 to 16 days. Neonates were admitted to department of pediatric surgery after sudden deterioration in health condition with distention and lividity of abdominal wall and retention of the gastric contents in gastric tube. Radiological image revealed signs of free air in the abdominal cavity (pneumoperitoneum) in 9 of 10 patients and airless abdomen in one case (fig. 1, 2).

Surgical treatment was used in all patients during 12 hours after recognition of the perforation. Nine of 10 patients were qualified for laparotomy.

In one preterm neonate with birth body weight 520 g being in extremely bad condition peritoneal drainage was performed in the neonatal department. Decreasing of the pressure in the abdominal cavity enabled the stabilization of child’s condition and delayed laparotomy performance.

Ileum perforation in nine of 10 patients were localized in a distance of 4 to 20 cm from ileocaecal valve. Jejunum perforation (primary and secondary) in 2 patients was localized 4 to 15 cm distally to Treitz ligament. Single changes 3 to 15 mm in diameter were present in 7 patients and multiple changes – in 3 patients. Macroscopic intraoperative assessment of the remaining segments of the intestine did not revealed inflammatory process (fig. 3).

Ileostomy was performed in 9 patients, in two patients with jejunum perforations end-to-end anastomosis was performed. Intestinal loop with multiple perforations was temporary exposed into the skin in 3 patients (fig. 4). Minimal range of surgical intervention was dictated by patient instability during the procedure.

Mean gestational age was 26.1 Hbd and mean birth body weight – 892 g. Bacteriological culture of peritoneal fluid revealed MR Staphylococcus sp in 5 of 10 patients and Candida sp in one patient. Histological assessment performed...
in 6 of 10 patients revealed haemorrhagic necrosis, lymphocyte infiltrations and focal thinning of intestine wall in one patient (fig. 5).

Enteral feeding after ileostomy procedure was introduced after restoration of intestinal peristalsis. Losses of proteins and electrolytes in 8 patients needed to be supplemented by parenteral nutrition during stoma maintenance. In a patient after primary jejunal anastomosis enteral nutrition was introduced 10 days after operation.

Ileostomy was maintained for 3 to 10 months. Survival rate in a study population was 80%. One child died before ileostomy closure due to secondary infection and the other died after ileostomy closure because of disseminated intravascular coagulation.

Follow-up period ranged from 4 to 24 months. Patients still are under our follow-up control and up today no surgical complications of gastrointestinal system were noted.

DISCUSSION

Increasing number of treated patients with SIP is related to the advances in perinatal care and intensive therapy in last years, not only from higher morbidity on SIP.

The relevant role in the pathogenesis of SIP plays the perinatal stress and hypoxia leading to perfusion disturbances and intestinal ischaemia and subsequently do limited perforation (9, 14). Etiology of SIP is unknown. Some authors do not even recognize SIP as separate disease entity qualifying it as benign form of NEC (9). Prematurity and related immaturity of digestive system, low Apgar scores, cardio-

respiratory resuscitation, peristalsis disturbances are the relevant factors of SIP development (13).

In our material Indomethacine and umbilical vessels cannulation are another important factors predisposing to SIP development. Nagaraj et al. described occurrence of intestinal perfusion disturbances after usage of indomethacine for PDA closure (10). Shorter et al. noted that earlier use of indomethacine after birth higher probability of intestinal perforation occurrence (11). In our material (10 patients with SIP) Ibuprofen for PDA closure was used in half of the patients. The suspicion arises that not only indomethacine but also other NSAIDs can influence the intestinal perforation.

The research of Mayer et al. suggest that micro-clots from catheters placed in the umbi-
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Lical vessels can cause ischaemia of the intestine wall and lead to the perforation (22). In our material umbilical vessels were cannulated in 8 patients. Umbilical vessel cannulation is widespread in the neonatal departments. It is suggested that appropriate care and shortening of the umbilical catheter holding could play a role in SIP prophylaxis.

Trophic feeding is a relevant factor in NEC development (85-95%) but its relation with SIP is not clear. Approximately 60% of patients with SIP is on parenteral nutrition and they do not receive any trophic feeding (4, 7, 12, 14). In our material trophic feeding was introduced in 5 of 10 patients.

Sudden onset is characteristic for SIP. Distention and lividity of abdominal wall are observed (4, 7, 9). That clinical presentation was noted in all of our patients.

In radiological images the most common is the presence of free air in abdominal cavity (pneumoperitoneum) and rarely airless abdomen. The lack of intestinal pneumatosis characteristic for necrotizing enterocolitis is an important finding in differential diagnosis (1, 4, 12, 13). In our study population typical radiological findings were present in 9 patients and air less abdomen in 1 case. None of our patients presence of gas vesicles either in portal vein or intestinal wall.

Laboratory tests usually reveal increased levels of inflammatory markers but they do not allow to differentiate SIP with other abdominal pathologies. The importance of cytokines (IL-8 i IL-10) and I-FABP (Intestinal Fatty Acid Binding Protein) levels characteristic for the early stage of intestine damage in NEC (17, 18).

Bacterial cultures of peritoneal fluid in SIP reveal most often the presence of Staphylococcus sp. Pumberger et al. describe common occurrence of fungal infections in patients with SIP which is suggested by other authors as the relevant factor of bad prognosis (4, 13). In our material bacteriological cultures of peritoneal fluid were positive for Staphylococcus sp. in 5 patients and for Candida sp. in 1 patient and in the other 4 cases were negative. In the neonate with fungal infection postoperative period was severe and complicated by secondary perforation of the jejunum (8 days after ileostomy).

Recognition of SIP is the indication for surgical treatment. Single or rarely multiple perforations 2-12 mm in diameter localized on the antimesentery edge of the terminal part of ileum are seen intraoperatively. The remaining segments of intestine are macroscopically unchanged (4, 13). In our material in 9 patients perforation was localized in ileum in a distance of 4-20 cm from ileocaecal valve. Multiple perforation was identified in 3 cases. Jejunum perforations were noted in 2 patients (primary perforation in one case and secondary in the other).

Surgical strategy in SIP is determined by general condition of the neonate. In the most severe cases the peritoneal drainage is used enabling for stabilization of the neonate condition and delayed laparotomy performance. In our material initial treatment with peritoneal drainage was performed in 1 preterm neonate (in the 16th day of life) being in the extremely bad condition. Stabilization of the child’s condition after three days enabled the performance of laparotomy. Restoration of the continuity of digestive system was performed in the 10th months of child’s life.

In selected cases peritoneal drainage can be final and effective treatment option for patients with SIP. In the opinion of Emil et al. that group of patients has low level of immature leucocytes in the blood smear and the lack of necessity to use of vasopressors.

It is estimated that up to 70% of patients treated with drainage, the delayed need laparotomy (23). In our patients peritoneal drainage was used to prepare for delayed laparotomy.

The most common procedure performed in neonates with SIP is two-stages operation. The first stage includes resection of the intestine with perforation with ileostomy performance. Haemodynamic instability during operation is the indication for temporary exposure of the intestine with perforations into the skin. The continuity of the digestive system was restored 3-6 months later which depended on patient’ general condition and his/her “tolerance” of intestine enterostomy (6, 13). In our material the primary ileostomy was performed in 6 patients. Intestinal loop with multiple perforations was temporary expose to the skin in 3 cases. The continuity of digestive system was restored 2-10 months after ileostomy performance (mean 3,5 months). Intolerance of ileostomy with losses of protein and electrolytes which needed to be supplemented parenteral nutrition, chronic inflammation around stoma,
technical and social problems and stenosis of stoma required ileostomy closure earlier. On the other hand coincident health problems delayed ileostomy closure. We do not observed simple coincidence between period of stoma and amount of peritoneal adhesions when ileostomy was closed.

Definitive one-stage treatment of SIP is performed in neonates in good general condition. It includes resection of the intestine with perforation and end-to-end anastomosis. But due to low birth body weight of the patient, lack of tightness and stenosis occurring in the anastomosis site in that group of patients, that surgery option is rarely performed (7). In our material end-to-end anastomosis was performed in 1 patient with primary perforation of the jejunum. In the recent literature there are some publications indicating the effectiveness of the drainage with drain T through the site of the perforation. Authors suggest that method can be used as primary and definite treatment option in SIP and also in the case of complications after primary anastomosis (19).

Final diagnosis of spontaneous intestinal perforation is confirmed by histological assessment. Lymphocyte infiltrations, haemorrhagic necrosis, muscle layer defect and multipole thin-walled vessels close to the perforation are characteristic findings in microscopic evaluation (6). In our material histological assessment was performed in 6 patients. Findings typical for SIP were found. In three cases after primary exposure of the intestinal loop with perforations a histological assessment revealed the healing evolution with no characteristic features of acute SIP was observed (fig. 6). In one patient 10 months after ileostomy exposed above the perforation side the short-distance intestinal stenosis in the inflamed segment of intestine was seen. In the histological assessment the granulation tissue and reparative processes after inflammation were detected (fig. 7).

The relevant factor for prognosis in SIP is frequent occurrence of other diseases in neonates with low birth body weight. The most important are concomitant neurological disturbances (intracranial haemorrhages, leucoma), respiratory distress (broncho-pulmonary dysplasia) and cardiologic disorders (congenital heart diseases). Taking into account above factors the outcome of surgical treatment of the patients with SIP is good. Survival rate ranges from 70 to 100% depending on the patient’s health condition and concomitant pathologies and is higher in patients with NEC treated surgically (12, 20). In a study group two neonates died due to generalized infection and disseminated intravascular coagulation. In the remaining 8 patients treating process was successfully terminated (restoration of the continuity of the digestive system) and we provide their follow-up.

**SUMMARY**

Due to rare prevalence of disease and advances in surgery techniques the summary of early and long term outcomes of different surgery treatments options in patients with spontaneous intestinal perforation in Poland has
not been yet established. Multicenter clinical studies could help with standardization of SIP treatment.

CONCLUSIONS

1. Risk factors for SIP development are prematurity, low birth body weight, umbilical vessels cannulation and pharmacological treatment of PDA.
2. Final diagnosis of SIP is confirmed by intraoperative intestinal findings and histological assessment.
3. Survival rate (80%) in study group correlated with individual surgical strategy and also advances in neonatal care.

REFERENCES

The Authors discuss a very important clinical problem of spontaneous intestinal perforation (SIP) in neonates. Etiology of SIP remains unclear. Among many established factors, prematurity seems to predispose to SIP although not every author of available publications shares this opinion. Most commonly a single or multiple site perforation is localized in the jejunum (as in the material presented in this paper) but literature reports data on a single site spontaneous gastrointestinal perforation along its whole length; its etiology may differ largely, depending on localization of the lesion.

Introduction to this paper is an extensive review of the SIP literature. A series of 10 cases of SIP treated by the Authors is too small to conduct any statistical analysis, however its description is a valuable contribution to a practical clinical knowledge about the course of this disease. SIP management used by the Authors does not differ from methods previously reported in the literature. Obtained results (survival 80% of affected neonates) do not differ from data obtained by established sites.

This paper is an original contribution of the Authors to the clinical knowledge in the area of spontaneous intestinal perforation which is more and more often encountered in the neonatal intensive care units. Although the paper does not provide new data on pathophysiology of SIP and does not report any new diagnostic or treatment methods, is one of few papers on this subject, reporting data obtained in quite large group of patients. Furthermore, the paper is of quite high didactic value.

Dr hab. Wojciech Dębek
Kierownik Kliniki Chirurgii Dziecięcej
Uniwersytetu Medycznego w Białymstoku