CASE REPORT

Acute appendicitis presenting as pneumoperitoneum in a teenage boy undergoing chemotherapy

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SUMMARY

Chemotherapy of paediatric haematological malignancies can induce infectious complications of the gastrointestinal tract, with predilection of the ileocaecal region. Common causes of right lower abdominal pain in the febrile patient with neutropaenia include acute appendicitis, typhlitis, ileus and intussusception. In this case report, we describe a teenage boy with acute appendicitis presenting with pneumoperitoneum during his course of chemotherapy. The incidence, aetiology, diagnosis, investigations and management of this uncommon presentation in a common disease are discussed. The controversial topic of the management of acute appendicitis in a febrile patient with neutropaenia is also reviewed and discussed.

BACKGROUND

Pneumoperitoneum is the presence of air in the peritoneal cavity. It is most frequently detected as free gas under the diaphragm in an erect plain X-ray if there is a significant amount of air present. Detection of small amounts of air requires a CT scan. The most common cause of pneumoperitoneum is a perforated abdominal viscus,¹ most frequently a perforated peptic ulcer. Furthermore, it has been shown that some chemotherapy agents increase the risk of development of peptic ulcers by inducing acute mucosal injury to the stomach and duodenum. However, in this article, to illustrate the possibility of alternative diagnoses in clinical practice, we present a teenage boy who developed pneumoperitoneum due to a different diagnosis while undergoing chemotherapy.

CASE PRESENTATION

A 10-year-old boy with acute lymphocytic leukaemia was admitted to the paediatric medical ward for chemotherapy with methotrexate, dexamethasone, L-asparaginase, vincristine and daunorubicin. During his hospitalisation and 2 weeks after administration of chemotherapy, he reported right-sided abdominal pain. Physical examination showed right-sided abdominal tenderness with guarding. He was afebrile and adequately hydrated, and his vital signs were stable. The blood pressure was 100/60 mm Hg and heart rate was 80 bpm. Blood tests revealed pancytopenia (white cell count $0.24 \times 10^9/L$, neutrophil $0.14 \times 10^9/L$, haemoglobin 8.9 g/dL, platelet $31 \times 10^9/L$), which was expected due to ongoing chemotherapy. Liver function test and amylase were normal. Renal function test

revealed normal creatinine level. Nonetheless, an erect abdominal X-ray showed free gas under the diaphragm (figure 1).

In view of the evidence of free intraperitoneal gas on abdominal X-ray and the history of chemotherapy, the top working diagnosis was a perforated peptic ulcer. Since frank peritoneal signs were present, the patient underwent an emergency operation without any further preoperative imaging such as ultrasound or CT of the abdomen and pelvis. Laparoscopy was arranged, and showed pus in the abdomen. The appendix was acutely inflamed and ruptured with abscess formation. There were also abscesses in the pelvis and the right paracolic gutter. Owing to the contamination of the peritoneal cavity, the assessment of the stomach and bowel was suboptimal. The operation was thus converted to open. With conversion to laparotomy for proper assessment, the stomach, duodenum and the rest of the bowel were found to be healthy. The air leak test for perforated peptic ulcer was negative. As the only pathology identified was an acutely inflamed appendix with a ruptured tip, leading to abscess formation and peritonitis, appendicectomy was performed. The appendix specimen showed an inflamed appendix with gangrenous change and a ruptured tip. There was no appendicolith. The peritoneal swab subsequently cultured *Escherichia coli*, *Pseudomonas aeruginosa*, *Klebsiella* spp, *Enterococcus* spp and *Bacteroides*. The patient was put on a full course of intravenous antibiotics (meropenem). He had an uneventful recovery and was resumed on chemotherapy on postoperative day 4.

Figure 1 Erect abdominal X-ray showing free gas under the diaphragm.

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DISCUSSION

On a review of the literature, two separate studies carried out on a total of 410 patients receiving either a combination of cyclophosphamide, methotrexate and 5-fluorouracil, or 5-fluorouracil alone, revealed that if gastroprotection with proton pump inhibitor was not provided, the risk of chemotherapy-induced gastroduodenal mucosal injury was significantly higher.^{2 3} The chemotherapy regimen of our patient was a combination of methotrexate, dexamethasone, L-asparaginase, vincristine and daunorubicin. Dexamethasone, being a steroid, is known to increase the risk of gastrointestinal perforation in hospitalised patients.^{4 5} Methotrexate has also been reported to cause severe intestinal injury in some patients.^{6 7} Therefore, given the above evidence, in a patient undergoing chemotherapy and presenting with pneumoperitoneum, the first diagnosis that comes to our mind would be a perforated peptic ulcer.

However, acute appendicitis is one of the most common diagnoses in acute surgical abdominal conditions. Clinical diagnosis is based on history, physical examination and investigations. The most common diagnostic imaging modalities include ultrasound and CT of the pelvis. Plain abdominal X-ray is seldom very informative unless it shows a radiopaque appendicolith.⁸ Free gas under the diaphragm is very rarely seen even if the appendix has perforated.^{1 9 10} Among the patients presenting with pneumoperitoneum, only 0–7% of cases can be attributed to a ruptured appendix.^{11 12} According to Spensley *et al*,¹³ radiographic findings of free air in the peritoneal cavity are usually caused by perforation of a peptic ulcer, but in 25–30% of cases, it results from other conditions such as perforated sigmoid diverticulum, leakage of intestinal anastomosis, etc. The unusual finding of intraperitoneal free gas in a ruptured appendix can mainly be explained by the pathogenesis of appendicitis. The mechanism responsible for acute appendicitis is obstruction of its lumen, either by lymphoid hyperplasia or a faecolith. Luminal obstruction leads to submucosal bacterial penetration and transmural suppurative necrosis of the appendicular wall. In early stages of appendicitis, there is oedema macroscopically with lymphoid hyperplasia and a neutrophil infiltrate microscopically. As the degree of inflammation progresses, this process will affect all the layers of the appendiceal wall and there will be a fibrinous exudate on the serosal surface. Ultimately, these will lead to gangrene and necrosis of the appendix, causing localised or generalised peritonitis. However, because of the luminal obstruction, luminal air does not usually pass into the peritoneal cavity. Therefore, radiological evidence of free peritoneal gas is rarely seen in perforated appendicitis.¹³ However, if present, the rare phenomenon of free intraperitoneal gas associated with ruptured acute appendix may be attributed to the escape of intestinal gas via the perforation site of the appendix or the production of gas by the periappendicular abscess bacteria.^{9 14 15} In our patient, the chemotherapy could have been an attributable factor for early rupture of the inflamed appendix as it contributes to mucosal injury. The absence of a faecolith allows the intraluminal gas to escape into the peritoneal cavity, leading to the presentation of pneumoperitoneum.

This case report demonstrates that perforated appendix is rarely the cause for pneumoperitoneum in the paediatric population, but it must be considered as one of the differential diagnoses and the appendix should be carefully inspected during laparoscopy or laparotomy, especially when other common pathologies of perforated viscus have been excluded.

Chemotherapy of paediatric haematological malignancies can induce infectious complications of the gastrointestinal tract, with predilection for the ileocaecal region. Common causes of right lower abdominal pain in the febrile patient with neutropaenia include acute appendicitis, typhlitis, ileus and intussusception.¹⁶ The management of acute appendicitis in the febrile patient with neutropaenia after intensive chemotherapy is controversial.¹⁷ The risks of delayed wound healing and infectious complications are higher in these immunocompromised individuals. Some authors advocate early appendectomy and aggressive surgical intervention,^{18–20} while some support conservative management with systemic antibiotics.¹⁷ Conservative management with systemic antibiotics and elective interval appendectomy have been reported as a feasible alternative for treatment of complicated appendicitis with delayed presentation in adult patients without malignancies.^{21 22} We have also experienced success with this treatment strategy in our paediatric patients who present with appendicitis complicated with abscess formation.²³ However, evidence of the efficacy and safety in delaying appendectomy for immunocompromised children with malignancies is generally lacking. In this particular patient, in view of the frank peritoneal signs and the radiological evidence of pneumoperitoneum, emergency laparotomy was arranged. However, in a stable patient with pneumoperitoneum on X-ray, but with clinical features in favour of acute appendicitis, a CT scan can be considered to better delineate the pathology. For immunocompromised patients at very high risk for operative intervention, conservative treatment with systemic antibiotics can be an alternative management strategy. Nevertheless, the best treatment option for such patients is still controversial. More experience and evidence are required to generate the perfect treatment protocol.

Patient's perspective

Patient:

- I was a bit nervous when I knew I had to undergo an operation as it was my first time going to the operating theatre, but I was not too scared or worried. I just wanted the operation to end as soon as possible so I could be pain-free. I think it was a memorable experience for me.

Parents:

- Our son was very brave in facing all the challenges during chemotherapy and the operation.

Learning points

- The usual presentation of a common disease as illustrated in this case reminds us of the possibility of alternative diagnoses in clinical practice.
- Acute surgical abdominal conditions are not uncommon in paediatric patients undergoing chemotherapy.
- These patients have higher risks of poor wound healing and postoperative complications. Whether or not and when to operate must be carefully considered for each individual patient.

Contributors CWYW wrote the case report. PHYC, LCLL and KKYW supervised CWYW.

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