

CLINICAL CASE

Acute abdomen as initial manifestation of M4 - acute non-lymphocytic leukemia

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Summary

Visceral involvement in acute non-lymphocytic leukemia (ANLL) seldom precedes hematological manifestation. We report on a patient with M4 - ANLL presenting with acute abdomen without any evidence of blood disorder. Laparotomy revealed only ileal wall oedema. Postoperative clinical deterioration led to a second-look operation combined with intraoperative endoscopy. Biopsied tissues were diffusely infiltrated by blasts characterised as HLA-DR (+), PGMI (50% +), MPO (50% +) and CD 34 (-). Bone marrow reconfirmed these findings and showed positivity for

CD4 (44%), CD11b (50%), CD11c (42%), CD13 (33%), CD34 (32%), and CD56 (54%). Chemotherapy achieved a complete but short remission. Relapse occurred 7 months later. Immediately after consolidation chemotherapy the profoundly immunosuppressed patient passed away after a lower respiratory tract infection. We discuss the contrast between histology and short disease duration, the unusual presentation and the bad prognosis, and attempt to correlate the clinical course with the coexpression of markers.

Key words: acute abdomen, acute non-lymphocytic leukaemia, CD11b, CD56, M4-ANLL

Case presentation

A 27-year-old male presented to our hospital with fever (38.7° C), productive cough, and vague abdominal discomfort for 7 days. He also reported weight loss of 8 kgs in the past 4 months. His medical history consisted only of an appendectomy for acute appendicitis 40 days ago in another hospital. On admission, physical examination was normal and with the exception of acute phase proteins, his laboratory findings were within normal range. Erythrocyte sedimentation

rate (ESR) was 52 mm/1st h (normal ≤ 20 mm) and C-reacting protein (CRP) 364 mg/L (normal 0-5 mg/L). Sputum Gram staining as well as urine and throat swab cultures were inconclusive. The following day acute abdominal pain and profound peritoneal irritation appeared while intestinal sounds diminished. His white blood cell (WBC) count rose to $17.1 \times 10^9/L$ with polymorphonuclear predominance and smear differentials showed a shift to the left but no blasts. Platelet count and blood biochemistry remained normal. Plain abdominal x-ray depicted air-fluid levels in the small intestine. Abdominal computerized tomography showed ileocecal wall thickening, surrounded by inflammatory elements and free fluid in the right paracolic gutter and the subhepatic space. The patient was forwarded to the operation theatre as "acute abdomen". Intraoperatively we met only a thickened and inflamed terminal ileum with multiple adhesions that were appropriately lysed. The various fluid samples collected intraoperatively were sterile. Recovery was quick but WBC, ESR and CRP remained abnormally high.

On the 5th postoperative day, fever and abdominal

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pain reappeared. Ultrasonography showed persistence of intestinal wall thickening and free fluid in the Douglas pouch, which was drained transcutaneously. This was sterile and contained 640 cells/mL, mostly mesothelial, without any cytologic evidence of malignancy. Barium enema showed an area of sigmoid with decreased motility while the terminal ileum could not be opacified. A colonoscopy to rule out inflammatory bowel disease reached only up to the transverse colon without detecting any abnormality. Several random sigmoid mucosal biopsies were unremarkable. General anaesthesia was employed for a push-through re-colonoscopy manually assisted through a small McBurney incision. This revealed a severely inflamed ileal mucosa, which was biopsied together with the mesentery, peritoneum, pre-peritoneal soft tissue and skin. Additionally, iliac crest bone and bone marrow were sampled. All samples were infiltrated by myeloid blasts with morphological and immunohistochemical characteristics of myelomonocytic ANLL – M4 (HLA-DR +, PGM1 50% +, MPO 50% + and CD 34 -) (Figure 1). Bone marrow was also diffusely infiltrated with more than 60% blasts differentiating up to the stage of promyelocyte, while all the 3 normal lines were suppressed. Bone marrow flow cytometry showed increased expression of CD4 (44%), CD11b (50%), CD11c (42%), CD13 (33%), CD34 (32%), CD56 (54%) and HLA-DR as in ANLL - M4. Karyotype was normal. Re-examination of the previous histology specimens (both appendix and sigmoid) failed to reveal any sign of acute leukemia.

A regimen based on Idarubicin and Ara-C achieved complete remission for 6 months. On relapse, a

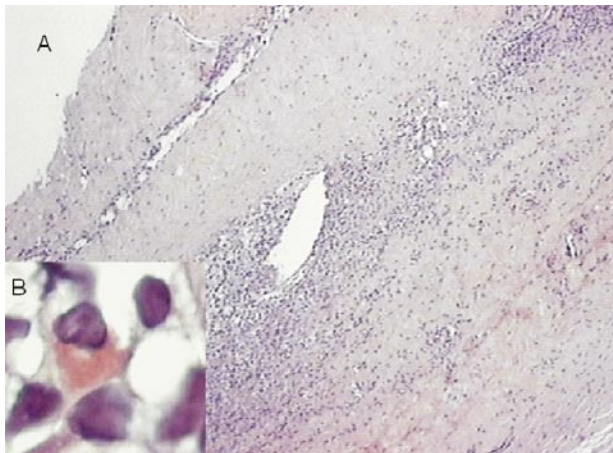


Figure 1. A: Connective tissue from the serosa of the bowel diffusely infiltrated by myeloid blasts (H&E $\times 25$). B (insert): Myeloid blast in bowel serosa (H&E $\times 630$).

high dose Ara-C consolidation cycle caused profound immunosuppression. The patient passed away after a severe lower respiratory tract infection.

Discussion

The usual manifestation of ANLL is through peripheral blood and bone marrow signs and symptoms. In advanced disease, abdominal viscera involvement may lead to conditions clinically appreciated as acute abdomen [1-6]. The opposite situation of visceral disease preceding haematological manifestation is rare.

Table 1 summarizes the existing literature on ANLL manifesting through gastrointestinal tract before any haematological sign in adults. Granulocytic sarcoma (chloroma), which is a solid tumor of leukemic tissue, seems to have been responsible in all cases. Such a solid tumor was not detected in our patient.

Acute abdomen as initial manifestation of ANLL has also been reported in a 10-year-old child with neutropenic enterocolitis (bacterial ileotyphlitis) [14]. This entity has an incidence around 5% in acute leukemia [3,6], and up to 21% in ANLL [5]. Furthermore, it has been implicated for up to 45% of the cases with acute abdomen in patients with known leukemia [2]. However, the microbial invasion into the intestinal wall which is supposed to be the principal pathogenetic mechanism was negated by our laboratory findings.

Peritoneal irritation in ANLL has also been correlated with petechial haemorrhage provoked by thrombocytopenia [15] while angiodescriptive features have been reported for the extramedullary lesions of CD56-positive patients [16] as in our case. Both the constantly high platelet number of our patient and our intraoperative and histological findings excluded this possibility also.

Finally, patients with known leukemia sporadically present with a "pseudo-acute" abdomen [1,9], a condition elicited by diffuse infiltration of the gastrointestinal tract, similar to the one we met. This infiltration has also been associated with gastrointestinal dysmotility (functional obstruction) [1,17], in line with our roentgenographic findings. In addition, the fast infiltration of the peritoneum and visceral serosa by blasts in our patient, as assumed by the wide dissemination of his disease in such a short time, would intensify peritoneal irritation, explaining the clinical setting. Moreover, its extramedullary presentation can be associated with the observed simultaneous expression of CD4 and CD56 (NCAM1) [18], while both the monocytic component of the blasts (M4) and the CD56 marker may correlate with the cutaneous involvement [16].

Table 1. Infiltration of the gastrointestinal tract as presenting manifestation of AML in adults

<i>Age/ Gender</i>	<i>Type</i>	<i>Tissues affected</i>	<i>Presenting symptoms</i>	<i>Initial treatment</i>	<i>Further treatment & outcome</i>	<i>Reference</i>
38/M	GS	Ileum, stomach	Obstruction	Rx	RDT – CMT, GS , AML	7
59/M	GS	Stomach	Pain, weight loss	Rx	AML, death (sepsis)	7
30/M	GS	Terminal ileum, cecum, omentum, perinodal adipose tissue	Pain, vomiting	Rx, RDT	GS, CMT, NED	8
16/F	GS	Small bowel, retroperitoneal lymph nodes	Abdominal distension, pain	CMT	NED	9
19/M	GS	Pericolonic adipose tissue, lymph nodes	Pain	CMT	NED	9
31/M	GS	Ileum, mesenteric adipose tissue	Pain, obstruction, rectal bleeding, weight loss	CMT	AML, CMT, NED	9
49/M	GS	Small intestine, mesentery	Pain, weight loss, obstruction	Rx, CMT	AML-M4Eo, CMT, BMT	10
38/F	GS	Terminal ileum	Obstruction	Rx, CMT	AML-M2, CMT, BMT	11
57/M	GS	Jejunum, retroperitoneum	Obstruction	Rx, RDT	AML-M2, death	12
34/M	GS	Ileum, mesentery	Obstruction	Rx	p.o. death (sepsis)	12
40/M	GS	Jejunum, mesenteric adipose tissue, lymph nodes	Obstruction	Rx, CMT	AML-M2, CMT, BMT, death (sepsis)	13
27/M	?	Small bowel, mesentery, parietal peritoneum, preperitoneal tissue, skin	Pain, fever	CMT	AML-M4, CMT, death (sepsis)	This case

GS: granulocytic sarcoma, Rx: surgical resection, CMT: chemotherapy, RDT: radiotherapy, p.o.: postoperative, BMT: bone marrow transplantation, NED: no evidence of disease, M: male, F: female

The relatively short remission period achieved by chemotherapy, and the bad prognosis thus implied, cannot be irrelevant to the unusual presentation of the malignancy or the speed of its dissemination. The existence of CD4, CD11b, concurrent HLA-DR and CD11b or CD56, all expressed in our patient, has been associated with lower percentages of complete remission and worse treatment response rates [19-22]. A relationship between these markers, either alone or in combination, and our patient's clinical course may exist. To our knowledge similar cases are not often described in the literature and a generalized conclusion cannot be drawn.

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