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Myeloid sarcoma and adenocarcinoma of the large bowel as collision tumors: a case report

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Summary. Myeloid sarcoma is a rare tumor composed of myeloid cells, localized in an extramedullary site, which may be associated with a concurrent myeloid neoplasm involving the bone marrow, although such an association is not required. Most patients present with acute myeloid leukemia and their prognosis is poor. We describe the case of a 76-year old woman with an adenocarcinoma of the right colon infiltrating the subserosa synchronous with a myeloid sarcoma at the same site; one pericolic lymph node was infiltrated by both tumors. The peculiarities of this case are the clinical presentation (as an acute abdomen due to subserosa infiltration by the myeloid sarcoma), the coexistence of a myeloid sarcoma with an adenocarcinoma of the right colon, and the absence of progression to acute leukemia. Coexistence of myeloid sarcoma and adenocarcinoma in the colon is probably incidental, and so it appears likely that the two different tumours arose from different mechanisms. However, a possible common background is conceivable. Some authors have found that p53 has a pivotal role in driving the maturation of myeloid stem cells and p53 is, also, involved in colon carcinogenesis. In our case, it may be hypothesized that synchronous heterogeneous mutations occurred in different types of committed cells or in stem cells secondary to p53 loss. Since only one case report has evaluated the correlation between myeloid sarcoma and adenocarcinoma of the large bowel, further immunohistochemical and molecular studies are needed to clarify the pathogenetic relationship between them.

Key words: Colon, Myeloid sarcoma, Adenocarcinoma, Collision tumors

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Introduction

Myeloid sarcoma (MS) also known as chloroma (King, 1853) or granulocytic sarcoma (Rappaport, 1966), is defined in the 2008 World Health Organization (WHO) classification of tumours of hematopoietic and lymphoid tissue (Pileri et al., 2008) as a tumor mass composed of myeloid blasts, with or without maturation, arising in extramedullary sites. It has been reported to occur in five conditions (Arber and Heerema-McKenney, 2011). In some cases MS may be a harbinger of acute myeloid leukemia (AML) in non-leukemic patients or can precede AML by months or years (Liu et al., 1973; Gunz and Baikle, 1974; Lin et al., 2008; Antic et al., 2010). In others it may herald a relapse in patients with previously treated disease. MS may also represent the acute blastic transformation of myelodysplastic syndromes (MDS) or myeloproliferative neoplasm (MPN) or MDS/MPN. The presence of MS is diagnostic of AML, regardless of bone marrow or blood status (Arber and Heerema-McKenney, 2011). However, in the vast majority of non-leukemic patients with myeloid sarcoma, acute leukemia develops within few months (mean 10.5-11 months) (Antic et al., 2010). It can occur virtually anywhere in the body and the most common sites of involvement in patients with no evidence of AML are bone, lymph nodes and skin (Mansi et al., 1987; Yamauchi and Yasuda, 2002; Tsimberidou et al., 2003). Other organs may be involved, such as the gastrointestinal tract (Toki et al., 1987; Antic et al., 2010), including, although very rarely, the large bowel (Matsunaga et al., 1991; Gorczyca et al., 1999; Lazaris et al., 2001; Akiyama et al., 2002; Makni et al., 2002; Antic et al., 2010; Benjazia et al., 2010). In the last case, MS always occurs concomitantly with or after the onset of AML. There is a predilection for males with a median age of 56 years (range, 1 month-89 years). The clinical

behavior and the response to therapy are not influenced by age, sex, anatomical site(s) involved, previous clinical history of AML, MDS, MPN, MDS/MPN, histological features, immunophenotype and cytogenetic findings (Pileri et al., 2008). Patients are commonly treated with induction chemotherapy followed by allogenic or autologous bone marrow transplantation. The percentage of successful long term treatment is very low (<10%) and treatment-related mortality can be high (>60%).

Herein we describe the case of a myeloid sarcoma of the right colon associated with an adenocarcinoma of the same site. To the best of our knowledge, this is the second case (Lazaris et al., 2001) of such an association and the first without progression to acute leukemia.

Materials and methods

Case report

A 79 year-old woman presented to the emergency care unit with a 5-day history of right lower quadrant abdominal pain accompanied by fever, nausea and vomiting. Patient suffered from hypertension and diabetes mellitus. CIRS (cumulative illness rating scale) for comorbidities evidenced a "frail" patient. Physical examination revealed a firm, distended abdomen with hypoactive bowel sounds, rebound tenderness, and guarding. There was no hepatosplenomegaly, lymphadenopathy, gingival hypertrophy or mucocutaneous petechiae. The patient presented with fever (body temperature 38°C). Laboratory data showed White blood count (WBC) of $15x10^9$/L (reference range: 4-$10x10^9$/L), with 86% neutrophils, 10% lymphocytes and 4% monocytes; Haemoglobin (Hb) 9.4 g/dL (reference range 13 to 18 g/dL); platelets $228x10^9$/L (reference range: $150x10^9$/L-$400x10^9$/L); Mean corpuscule volume (MCV) 67 (reference range 80 to 100 fL); and ferritin 12 (reference range 10 to 300 ng/nL). These results evidenced a multifactorial anaemia (microcitic anaemia due to iron deficiency plus anaemia due to inflammation). Abdominal radiographic examination showed multiple air fluid levels and dilated loops of the large bowel. Given the severity of presentation with symptoms of acute abdomen, the patient underwent urgent right hemicolectomy with end ileostomy. A diagnosis of myeloid sarcoma associated and intermingled with moderately differentiated adenocarcinoma [pT3N1aM0 (AJCC-UICC 2010), C2 (Dukes)/IIIB (TNM7) G2 (WHO 2010)] was made. The patient had intestinal and wound bleeding lasting two months after surgery, complicated by infection and necrosis of the abdominal wall. Considering that the patient's conditions and comorbidities limited every possible chemotherapy for MS and adenocarcinoma, the patient was supported only with erythropoietin stimulating agents (ESA) and iron IV, helping her to avoid red blood cell transfusions. A bone marrow biopsy (BM-1), performed one week after the surgery, was almost normal. Considering the histological diagnosis, the BM biopsy was repeated after six months. The BM-2 was suggestive of a myelodisplastic syndrome (refractory anaemia with excess blasts-RAEB1). Fourteen months later, the patient's blood count worsened revealing a WBC of $36.2x10^9$/L (neutrophils 40%, lymphocytes 13%, monocytes 20%, myelocytes 10%, metamyelocytes 8%, promyelocytes 9%) with $509x10^9$/L platelets and Hb level reduction (8.9 g/dL). A bone marrow biopsy established a diagnosis of a myelodysplastic/myeloproliferative neoplasm (type 2 chronic myelomonocytic leukemia). Hydrocarbamide 500 mg/day was started to help to control leucocytosis and ameliorating haemoglobin levels. The patient is still in good condition at 36 months of follow-up.

Methods

The large bowel specimen consisted of a right hemicolectomy (24 cm) and a terminal ileum resection (7 cm). Pericolic and peri-ileal tissues and several lymph nodes were also dissected. Representative samples were fixed in 10% buffered formalin and embedded in paraffin. Histological sections (4 μm thick) were stained with hematoxylin and eosin and examined by light microscopy. For immunohistochemical stains the Ultravision Detection System antiPolyvalent HRP (LabVision, Fremont, CA, USA; Bioptica) was employed, using diaminobenzidine (DAB; Dako) as the chromogen. The following antibodies were checked: CD34, CD43, CD10, CD20, CD3, CD56, MPO, CD123, CD68, CD68PGM1, CD117, TdT, BDCA-2/CD303, TCL1, p53, NPM1 and Mib-1. Bone marrow biopsies were previously placed into B5 fixative for 1-2 hours, washed in tap water for 2-3 minutes and decalcified for 20 to 40 minutes. Then, they were employed in 10% buffered formalin until ready to load into the processor. Cytogenetic analysis was performed with a Wright-Giemsa banding technique on bone marrow aspirate. Metaphase cells from short-term unstimulated cultures at 37°C in RPMI-1640 medium, supplemented with 10% fetal calf serum, were examined. Chromosomal abnormalities were described according to the International System for Human Cytogenetic Nomenclature (ISCN 2009). Fluorescence in situ hybridization (FISH) was done utilizing the following probes: MLL break apart (11q23), LSI CBFB (inv 16) dual color, LSI AML1 ETO (t 8;21), CEP 8.

Results

Grossly, the right colon showed an ulcerated cauliflower-like lesion (2,5 cm in greater dimension) located 10 cm from the ileal margin, extending transmurally through all the intestinal layers until the subserosa. The colon wall appeared rigid and thickened; pericolic and peri-ileal fatty tissues were firm and lymph

nodes were enlarged. Microscopically, a moderately differentiated adenocarcinoma infiltrating the subserosa was observed (Fig. 1A). Inside and outside the adenocarcinoma a population of cells with blastic appearance, thin nuclear membrane, round nuclei, finely dispersed chromatin, single or multiple small central nucleoli, and scant basophilic cytoplasm were detected (Fig. 1B,C). Some granulocytes with variable differentiation were also seen, which were mostly mature eosinophils. Blast-like cells and mature granulocytes diffusely infiltrated pericolic stromal tissues. Lymph node architecture was effaced by infiltration of both the adenocarcinoma and myeloid sarcoma (Fig.1D). Blast-like cells strongly expressed CD43 (Fig. 2A), CD68 (Fig. 2B), CD68PGM1, MPO (Fig. 2C) while they were negative for CD34, TdT, CD10, CD20, CD3, CD56 (Fig. 2D), CD117, CD123, BDCA-2/CD303, TCL1 and NPM1; p53 was positive both in adenocarcinomatous and in blast-like cells. There were scattered mitotic figures and the proliferative rate (Mib-1) was of 50-60%.

BM-2 showed alteration of the normal histotopography with hypercellularity (Fig. 3A), and multilineage dysplasia. The erythropoiesis was increased and the erythroid precursors displayed dyserythropoiesis. Granulopoiesis was also amplified with 5-9% of CD34 positive blasts (Fig. 3B), they were mainly myeloblasts. Some micromegakaryocytes were observed. An increase of iron deposits was demonstrated by Perls stain. A diagnosis of RAEB1 was performed. Cytogenetic analysis on BM-2 cells showed a normal karyotype: 46,XY [20 cells]. The bone marrow at month 14 (BM-3)

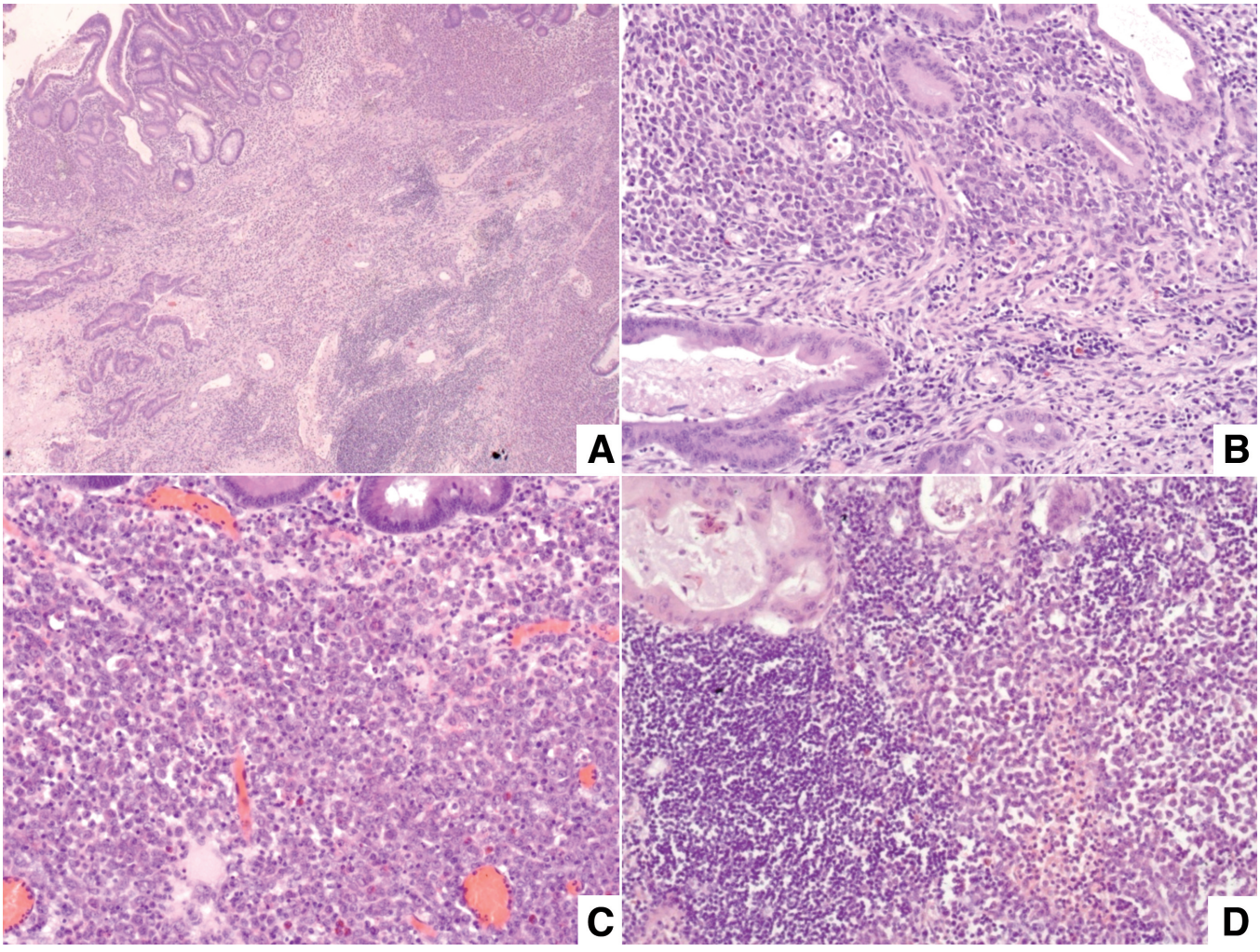

Fig. 1. Moderately differentiated adenocarcinoma infiltrating the subserosa associated to a proliferation of cells with blastic appearance is observed **(A)**. Blastic cells showing round, irregular nuclei, finely dispersed chromatin, a single or multiple small central or paracentral nucleoli, and scant eosinophilic or basophilic cytoplasm **(B-C)**. A pericolic lymph node infiltrated by both tumors **(D)**. H&E. A, x 5; B-D, x 10

was hypercellular (Fig. 3C) with multilineage dysplasia. Granulocytic proliferation was increased with 10-15% of CD34 positive blasts (Fig. 3D). Micromegakaryocytes and megakaryocytes with a tendency to form clusters were also observed. A moderate increase in the amount of reticulin fibres was present. CD68PGM1 showed a high number of monocytes (30%). A diagnosis of MDS/MPN (type 2 chronic myelomonocytic leukemia-CMML) was made. Cytogenetic analysis on BM-3 cells showed 46,XX 47,XX,+8. Moreover, a trisomy of chromosome 8 was confirmed in 25% of 200 total cells scored by two independent observers. Given the particular interesting clinical presentation and the concomitant diagnosis of MS and adenocarcinoma in the colon, and the presence of a myeloid clone in the BM-3, we looked back at the stored diagnosis BM-1 and BM-2 performed FISH utilizing CEP 8 probe looking for an occult trisomy 8; FISH was normal again for chromosome 8 on 500 cells scored. Afterwards, we performed FISH on a thin section of the paraffin embedded colon tissue, looking for chromosomal abnormalities in the initial myeloid sarcoma. FISH showed a +8 in 15% of the cells (Fig. 4).

Discussion

MS is defined as an isolated or multiorgan invasive and destructive tumor composed of immature cells of myeloid series, localized in extramedullary sites (Pileri et al., 2008). An accurate revision of the literature showed us that almost all cases of MS are related to the development of haematological disorders although Pileri et al. (2007) reported 25 de novo cases of MS out of 92. In the case herein illustrated AML did not develop during 36 months of follow-up after the diagnosis and the patient is still with a stable disease. Regardless of the

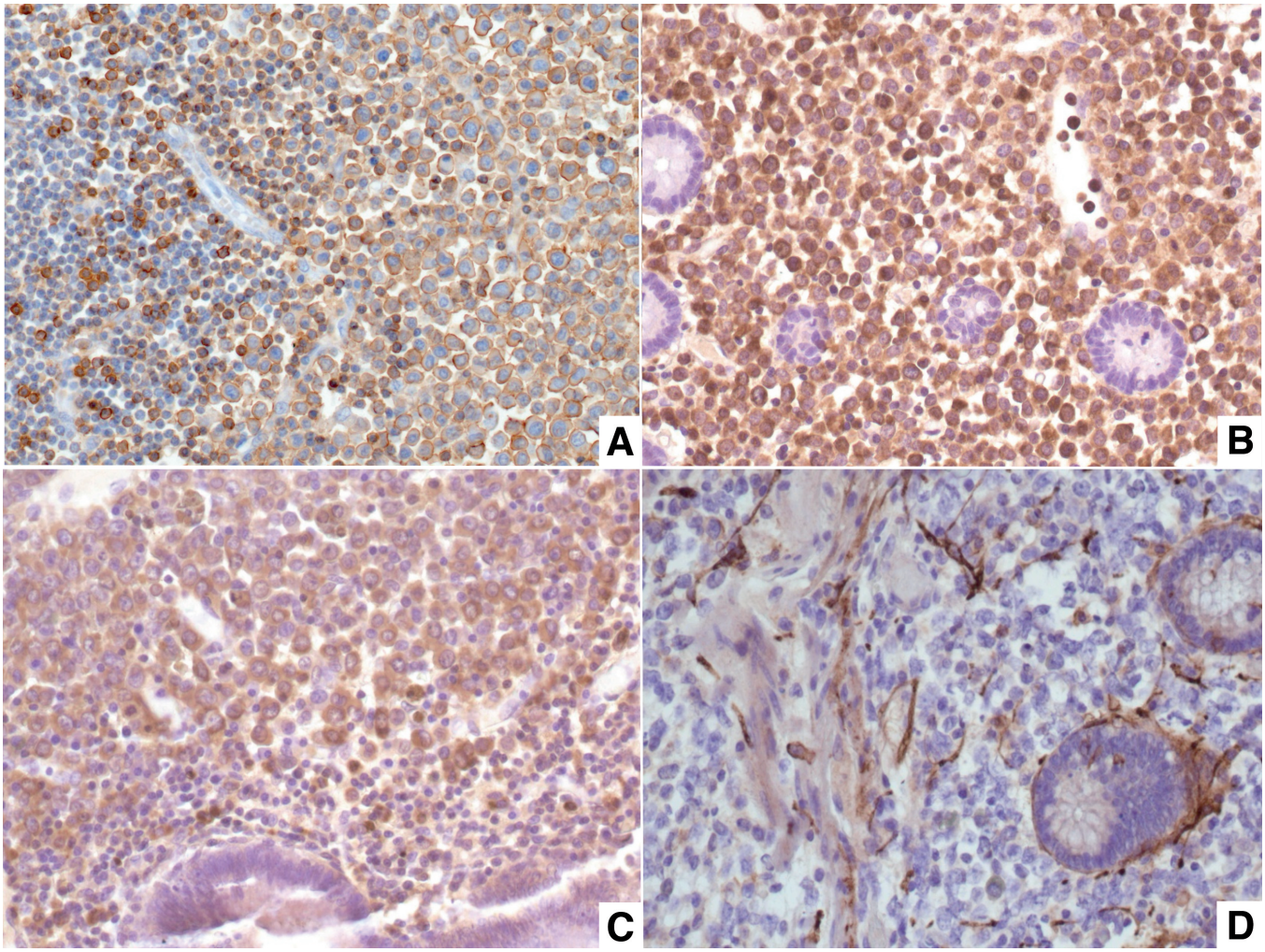

Fig. 2. Blast-like cells strongly express CD43 **(A),** CD68 **(B)** and MPO **(D)** whereas they are negative for CD56 **(D)**. x 20

site, MS are difficult to recognize because the majority of them do not produce specific clinical signs and symptoms. In our case, the patient presented with symptoms of acute abdomen. The histopathological diagnosis of MS may be difficult because its cell population varies from well-differentiated to poorly differentiated cells. In a significant proportion of cases, it displays myelomonocytic or monoblastic morphology. In this case, the diagnosis is worthy and can be facilitated by immunohistochemistry. In fact, the marker combination allows the recognition of tumours with a more immature myeloid phenotype, as well as of cases with myelomonocytic, monoblastic, erythroid or megakaryocytic differentiation (Pileri et al., 2008). Up to 75% of cases of isolated myeloid sarcoma are misdiagnosed as malignant lymphoma (Antic et al., 2010), in particular, diffuse large B cell lymphoma, lymphoblastic lymphoma, Burkitt lymphoma, anaplastic large cell lymphoma or as small round cell tumors or as blastic plasmacytoid dendritic cell neoplasm (Meis et al., 1986; Menasce et al., 1999). In about 50% of cases of myeloid sarcoma, several chromosomal aberrations have been detected. The most common are t(8;21), t(15;17), inv(16) (Deeb et al., 2005); other abnormalities include monosomy 7 and 16, trisomy 4, 8 and 11 (Pileri et al., 2007). Interestingly, the presence of inv(16)(p13;q22) or the related t(16;16)(p13;q22) has been found in the presence of intestinal involvement. About 16% of cases carry evidence of NPM1 mutation as shown by aberrant cytoplasmic NPM expression (Falini et al., 2005, 2007). In our case, trisomy 8, which is rarely described in MS (10% of cases) (Deeb et al., 2005), was evidenced in the bone marrow concomitantly with the diagnosis of MDS/MPD (14 months after the diagnosis of MS). The

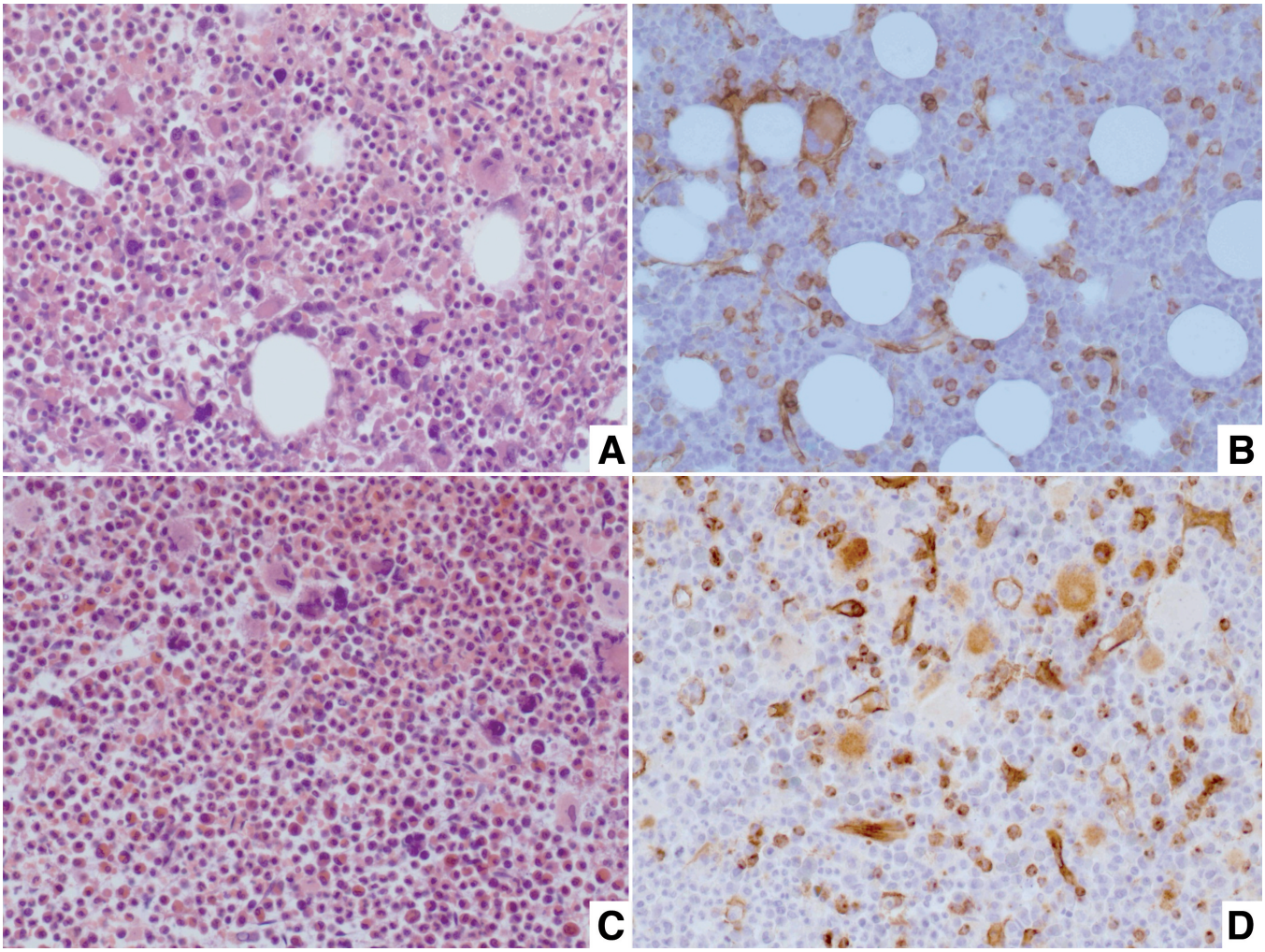

Fig. 3. Hypercellularity, multilineage dysplasia and dyserithropoiesis with micromegakariocytes (**A**, H&E) and blasts CD34 positive **(B)** are observed. Granulocytic proliferation and dysgranulopoiesis are present (**C**, H&E) with micromegakariocytes forming cluster and CD34 positive blasts **(D)**. x 20

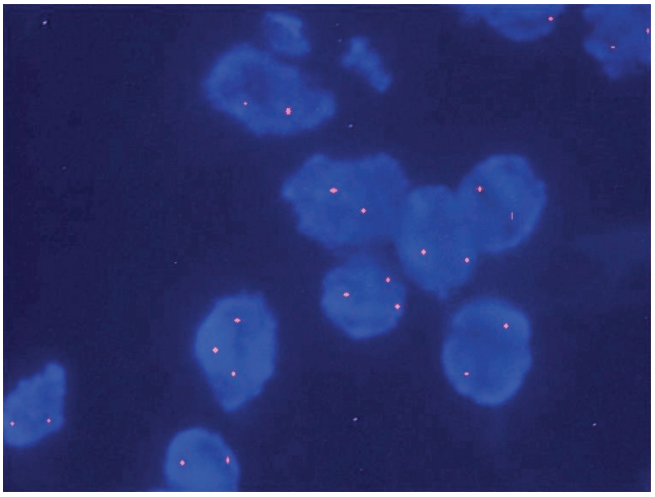

Fig. 4. FISH on paraffin embedded colon tissue showing leukemic interphase cells. CEP 8 probe is labeled in red, trisomy 8 is present in cells with three red spots, while normal diploid chromosome 8 number is present in cells with two spots.

presence of the same clone was also demonstrated subsequently in the myeloid sarcoma cells in the initial colon specimen but not in BM-1 and BM-2 cells. This may mean that there was a spread of the neoplastic clone from colonic MS to bone marrow, giving rise to MDS/MPD. The normal appearance of the bone marrow at the time of the diagnosis of MS, seems to be in favor of such a hypothesis, although further studies are necessary to confirm that. In the literature the onset of CMML in a patient with a previous history of RAEB was exceptionally reported (Kadowaki et al., 1988); instead Breccia et al. (2008) described a series of 16 patients who were originally diagnosed having RAEB but later developed peripheral monocytosis, leading to their reclassification in CMML. These patients have a more favorable prognosis and prolonged survival by comparison with those with RAEB. CMML and MDS may share similar features, which renders it difficult to distinguish one from the other. However, despite the similarities, if the WHO criteria are carefully applied (Orazi et al., 2008), the finding of monocytosis of at least $1x10^9$/L is sufficient for a diagnosis of CMML rather than MDS (Head and Hamilton, 2011; Hyek and Vardiman, 2011). Considering these facts, in our case, we are in favor of a CMML developing from a RAEB1. The eventual role of trisomy 8 in the clinical and prognostic behavior of MS remains to be elucidated. An early diagnosis of myeloid sarcoma is of great importance in the ongoing management of this malignancy: in fact, 80% to 90% of cases of myeloid sarcoma without an overt leukemic syndrome progress to AML within 10.5-11 months from the diagnosis (Lin et al., 2008). For this reason, it has been sometimes recommended to treat patients (chemotherapy and/or external radiation, and allogenic/autologous bone marrow transplantation) also for AML independently of its presence at the time of diagnosis to improve prognosis (Breccia et al., 2003; Sevinc et al., 2004). In our case, patient's clinical conditions and comorbidities were life threatening at diagnosis, limiting every possible therapy both for adenocarcinoma and for MS. Moreover, in Italy MS associated with MDS and/or MDS/MPN is usually not treated intensively or in an aggressively way when present in elderly people, favoring a less intense chemotherapy. The percentage of successful long term treatment is very low (<10%) and treatment-related mortality can be high (>60%).

The coexistence of MS and adenocarcinoma could be incidental since we cannot demonstrate a similar origin. Nevertheless, specific genetic aberrations occurring at gene loci with high proximity might, hypothetically, form the basis of this coexistence. A review of previously reported MS has shown abnormalities involving chromosome 17, in which the p53 tumor-suppressor gene is located; the latter gene is known to be implicated in colorectal carcinogenesis (Lazaris et al., 2001). In our case, karyotype analysis did not show any abnormalities of chromosome 17 but immunohistochemistry for p53 was positive both in adenocarcinomatous and in MS cells. Recent studies have linked p53 to the process of stem-cell self-renewal such that loss of p53 counters for the deleterious effects of oncogenic k-ras on these cells and enables them to self-renew indefinitely (Zhao et al., 2010). We can speculate that the occurrence of p53 loss in intestinal stem cells determined the development of the two malignancies in the same site. Moreover, additional chromosomal aberrations in myeloid committed cells (e.g. 8 trisomy) could eventually select a neoplastic clone that migrated into BM inducing the evolution of a MDS in a MDS/MPN.

In conclusion, further clinical, immunohistochemical and molecular studies are needed to clarify the pathogenetic relationship between adenocarcinoma and MS as collision tumours in large bowel.

References

Akiyama N., Ohwada A., Kajiwara K., Ohtake H., Hayama M., Kohri M., Taira M., Niitsu N., Horie R. and Higashihara M. (2002). Granulocytic sarcoma of the colon in chronic myelomonocytic leukemia. Rinsho Ketsueki. 43, 937-942.

Antic D., Elezovic I., Bogdanovic A., Vukovic N.S., Pavlovic A., Jovanovic M.P., Jakovic L. and Kraguljac N. (2010). Isolated myeloid sarcoma of the gastrointestinal tract. Intern Med. 49, 853-856.

Arber D.A. and Heerema-McKenney A. (2011). Myeloid neoplasms. In: Hematopathology. 1st ed. Jaffe E.S., Harris N.L., Vardiman J.W., Campo E. and Arber D.A. (eds). Elsevier Saunders. St. Louis. pp 694-697.

Benjazia E., Khalifa M., Benabdelkader A., Laatiri A., Braham A., Letaief A. and Bahri F. (2010). Granulocytic sarcoma of the rectum: report of one case that presented with rectal bleeding. World J.

Gastrointest. Pathophysiol. 1, 144-146.

Breccia M., D'Andrea M., Mengarelli A., Morano S.G., D'Elia G.M. and Alimena G. (2003). Granulocytic sarcoma of the pancreas successfully treated with intensive chemotherapy and stem cell transplantation. Eur. J. Haematol. 70, 190-192.

Breccia M., Cannella L., Frustaci A., Stefanizzi C., D'Elia G.M. and Alimena G. (2008). Chronic myelomonocytic leukemia with antecedent refractory anemia with excess blasts: further evidence for the arbitrary nature of current classification system. Leuk. Lymphoma 49, 1292-1296.

Deeb G., Baer M.R., Gaile D.P., Sait S.N., Barcos M., Wetzler M., Conroy J.M., Nowak N.J., Cowell J.K. and Cheney R.T. (2005). Genomic profiling of myeloid sarcoma by array comparative genomic hybridization. Genes Chromosomes Cancer 44, 373-383.

Falini B., Mecucci C., Tiacci E., Alcalay M., Rosati R., Pasqualucci L., La Starza R., Diveiro D., Colombo E., Santucci A., Bigerna B., Pacini R., Pucciarini A., Liso A., Vignetti M., Fazi P., Meani N., Pettirossi V., Saglio G., Mandelli F., Lo-Coco F., Pelicci P.G. and Martelli M.F. (2005). Cytoplasmic nucleophosmin in acute myelogenous leukemia with a normal karyotype. N. Engl. J. Med. 352, 254-266.

Falini B., Lenze D., Hasserjian R., Coupland S., Jaehnne D., Soupir C., Liso A., Martelli M.P., Bolli N., Bacci F., Pettirossi V., Santucci A., Martelli M.F., Pileri S. and Stein H. (2007). Cytoplasmic mutated nucleophosmin (NPM) defines the molecular status of a significant fraction of myeloid sarcoma. Leukemia 21, 1566-1570.

Gorczyca W., Weisberger J. and Seiter K. (1999). Colonic adenomas with extramedullary myeloid tumor (granulocytic sarcoma). Leuk. Lymphoma 34, 621-624.

Gunz F. and Baikle A.G. (1974). Leukemia. 3rd ed. Grune and Stratton. New York. p 282.

Head D.R. and Hamilton K.S. (2011). The myelodisplastic syndrome. In: Hematopathology. 1st ed. Jaffe E.S., Harris N.L., Vardiman J.W., Campo E. and Arber D.A. (eds). Elsevier Saunders. St. Louis. pp 656-671.

Hyek E. and Vardiman W. (2011). Myelodisplastic syndrome/ Myeloproliferative neoplasms. In: Hematopathology. 1st ed. Jaffe E.S., Harris N.L., Vardiman J.W., Campo E. and Arber D.A. (eds). Elsevier Saunders. St. Louis. p 746.

Kadowaki N., Kamesaki H., Ohno Y., Amano H., Imanaka T., Takahashi Y. and Kobashi Y. (1988). Chronic myelomonocytic leukemia evolved from refractory anemia with excess of blasts, associated with karyotypic abnormality and marked monocytosis. Rinsho Ketsueki. 29, 2145-2151.

King A. (1853). A case of chloroma. Monthly J. Med. 17, 97.

Lazaris A.C., Papanikolaou I.S. and Xirou P.A. (2001). Coexistence of a granulocytic sarcoma and adenocarcinoma of the rectum. Am. J. Gastroenterol. 96, 615-616.

Lin C.H., Wu K.H., Lin W.C., Tsai J.D., Peng C.T. and Chen A.C. (2008). Granulocytic sarcoma of the colon in a child with acute myeloid leukemia presenting as hematochezia. J. Pediatr. Hematol. Oncol. 30, 981-983.

Liu P.I., Ishimaru T., McGregor D.H., Okada H. and Steer A. (1973). Autopsy study of granulocytic sarcoma (chloroma) in patients with myelogenous leukemia, Hiroshima-Nagasaki 1949-1969. Cancer 31, 948–955.

Makni S., Bahri I., Ayadi L., Mseddi A., Bouaziz M. and Jlidi R. (2002). Colonic granulocytic sarcoma: a case report. Ann Chir. 127, 480-483.

Mansi J.L., Selby P.J., Carter R.L., Powles R.L. and McElwain T.J. (1987). Granulocytic sarcoma: a diagnosis to be considered in unusual lymphoma syndromes. Postgrad. Med. J. 63, 447-449.

Matsunaga T., Maseki N., Kaneko Y., Sampi K., Tsuchimochi T., Sakurai M. and Hattori M. (1991). An 8;21 chromosome translocation associated leukemia presenting with large intestinal granulocytic sarcoma: a report of two cases. Rinsho Ketsueki. 32, 782-785.

Menasce L.P., Banerjee S.S., Beckett E. and Harris M. (1999). Extra-medullary myeloid tumour (granulocytic sarcoma) is often misdiagnosed: a study of 26 cases. Histopathology 34, 391-398.

Meis J.M., Butler J.J., Osborne B.M. and Manning J.T. (1986). Granulocytic sarcoma in nonleukemic patients. Cancer 58, 2697-2709.

Orazi A., Bennet J.M., Germing U., Brunning R.D., Bain B.J. and Thiele J. (2008). Chronic myelomonocytic leukemia. In: WHO Classification of tumours of haematopoietic and lymphoid tissue. 4th ed. Swerdlow S.H., Campo E., Harris N.L., Jaffe E.S., Pileri S.A., Stein H., Thiele J. and Vardiman J.W. (eds). IARC. Lyon. pp 76-79.

Pileri S.A., Ascani S., Cox M.C., Campidelli C., Bacci F., Piccioli M., Piccaluga P.P., Agostinelli C., Asioli S., Novero D., Bisceglia M., Ponzoni M., Gentile A., Rinaldi P., Franco V., Vincelli D., Pileri A. Jr, Gasbarra R., Falini B., Zinzani P.L. and Baccarani M. (2007). Myeloid sarcoma: clinico-pathologic, phenotypic and cytogenetic analysis of 92 adult patients. Leukemia 21, 340-350.

Pileri S.A., Orazi A. and Falini B. (2008). Myeloid sarcoma. In: WHO Classification of tumours of haematopoietic and lymphoid tissue. 4th ed. Swerdlow S.H., Campo E., Harris N.L., Jaffe E.S., Pileri S.A., Stein H., Thiele J. and Vardiman J.W. (eds.). IARC. Lyon. pp 140-141.

Rappaport H. (1966). Tumors of the hematopoietic system. Atlas of tumors pathology. Section III. Fascicle 8. Armed Forces Institute of Pathology. Washington. pp 241–243.

Sevinc A., Buyukberber S., Camci C., Koruk M., Savas M.C., Turk H.M., Sari I. and Buyukberber N.M. (2004). Granulocytic sarcoma of the colon and leukemic infiltration of the liver in a patient presenting with hematochezia and jaundice. Digestion 69, 262-265.

Toki H., Okabe K., Kimura Y., Kiura K., Shibata H., Hara K., Moriwaki S., Nanbu T. and Iwashita A. (1987). Granulocytic sarcoma of the intestine as a primary manifestation nine months prior to overt acute myelogenous leukemia. Jpn. J. Clin. Oncol. 17, 79-85.

Tsimberidou A.M., Kantarjian H.M., Estey E., Cortes J.E., Verstovsek S., Faderl S., Thomas D.A., Garcia-Manero G., Ferrajoli A., Manning J.T., Keating M.J., Albitar M., O'Brien S. and Giles F.J. (2003). Outcome in patients with nonleukemic granulocytic sarcoma treated with chemotherapy with or without radiotherapy. Leukemia 17, 1100-1103.

Yamauchi K. and Yasuda M. (2002). Comparison in treatments of nonleukemic granulocytic sarcoma: report of two cases and a review of 72 cases in the literature. Cancer 94, 1739-1746.

Zhao Z., Zuber J., Diaz-Flores E., Lintault L., Kogan S.C., Shannon K. and Lowe S.W. (2010). p53 loss promotes acute myeloid leukemia by enabling aberrant self-renewal. Genes Dev. 24, 1389-1402.

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