Case report

Coexistence of a granulocytic sarcoma and adenocarcinoma of the rectum

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SUMMARY

Granulocytic sarcomas are rare extramedullary tumour-like proliferates of myelogenous precursor cells. Rarely, these tumours may de novo precede acute leukaemia or represent the initial manifestation of a blast crisis in the course of a chronic myeloproliferative disease. A case of a 53 year old male who was admitted to hospital due to intestinal bleeding combined with weight loss is reported. General examination, laboratory studies and imaging findings were nonspecific. Colonoscopy revealed a rectal polypoid mass. Microscopic pathology and immunohistochemical findings were consistent to that of a collision tumour composed of rectal adenocarcinoma arisen on a pre-existing adenomatous polyp and granulocytic sarcoma. Two months later he was readmitted to hospital and the diagnosis of acute myetoid leukaemia was established. The patient finally died due to infection. Coexistence of rectal adenocarcinoma and granulocytic sarcoma should be recognized promptly so that proper therapy is initiated, thus improving prognosis.

Keywords: granulocytic sarcoma, rectal adenocarcinoma, acute myeloid leukaemia, immunohistochemistry.

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INTRODUCTION

Granulocytic sarcoma is a rare extra-medullary tumour mass of myeloid precursor cells, which may occur before, simultaneously or after the diagnosis of acute myeloid leukaemia (AML) or other myeloproliferative disorders.[1] Differential diagnosis may be difficult, especially in the absence of concurrent haematological disease. The tumour may be located in several extra-medullary sites, rarely involving the large intestine.[2,3] Coexistence of the tumour with other solid tissue malignancies is very rare.[4,5] We report a case of a patient who was admitted to hospital due to intestinal bleeding. Endoscopy revealed a rectal mass. In the colectomy surgery specimen, pathologic examination and immunohistochemistry confirmed the presence of an adenocarcinoma of the rectum and a coexisting granulocytic sarcoma.

CASE REPORT

A 53 year old white male was admitted to hospital due to intestinal bleeding the 4 days preceding his admission and a weight loss of 10 kg* in the previous month. General examination, a complete blood cell count, blood chemistry and coagulation studies were normal, except for anaemia (haematocrit, 34%) and a mild increase in the white blood cell count. The erythrocyte sedimentation rate was also elevated (53 mm/h). The patient was referred to the endoscopy department and colonoscopy revealed a rectal polypoid mass. Microscopic pathology of the biopsies taken from the mass was consistent to that of an adenocarcinoma. A chest x-ray and an abdominal computed tomography scan were normal. Left colectomy was performed. Grossly, in the colectomy surgical specimen, a 3.5 cm in diameter polypoid lesion with a focally greenish cut surface was observed. At first inspec-

tion, the microscopic pathology of the tumour was that of a grade I (well-differentiated) adenocarcinoma extending through the submucosa in the inner circular layer of the muscularis extema. There was evidence of adenomatous remnants in the superficial part of the tumour. Additionally, a diffuse monotonous infiltrate of medium-sized cells often associated with a sprinkling of cells containing eosinofilic granules was observed through the entire intestinal wall (Figure 1) as well as into the pericolonic fat. All four tumour adjacent lymph nodes (measuring less than 0,8 cm in maximum diameter) demonstrated partial effacement of their architecture with predominant involvement of the sinuses by these cells. The latter were focally characterized by larger nuclei and high mitotic counts. Naphthol AS-D chloroacetate esterase (NASD-CAE) staining was positive. Immunohistochemical stains including myeloperoxidase (MPO) (Figure 2), lysozyme, CD43 and CD68 were positive. T- and B-cell markers (CD3, CD45 and CD20 respectively) as well as CD30 were negative. These findings confirmed the diagnosis of a coexisting granulocytic sarcoma. P53 protein expression was also investigated by using the monoclonal mouse anti-human p53 protein antibody (clone D07, DACO, Glostrup, Denmark).

Two weeks after diagnosis, a complete blood cell count was performed, which revealed anaemia (haematocrit, 31%) and the presence of blasts in a proportion of 8-10% in the peripheral blood. A bone marrow aspirate was suggestive of myelodysplastic syndrome (MDS) in transformation, due to the high blast percentage (25%). According to the proposed World Health Organization classification, the present syndrome was classified as refractory anaemia with excess blasts, type 2 (RAEB-2). In detail, in the blood smear, the red blood cells showed increased anisocytosis and poikilocytosis with macrocytes including dacryocytes; neutrophil abnormalities included pseudo-Pelger-Huet nuclei and hypogranulation. In the bone marrow smear, apart from the above mentioned increase in myeloblasts, the presence of Auer rods in them, as well as an increase in promyelocytes were noticeable; erythroid abnormalities included megaloblastoid nuclei and presence of ringed sideroblasts; numerous micromegacaryocytes were also observed.

The patient seeked further consultation in another medical institution and was discharged from our hospital, but was readmitted two months later due to fever, dyspnea and an 8-kg* weight loss. Blood cell counts, flow cytometry analysis and a bone marrow biopsy which were performed, established the diagnosis of acute myeloid leukemia (AML). The patient remained febrile and his condition steadily deteriorated. Blood cultures drawn at admission were positive for *Pseudomonas aeruginosa.* Despite antibiotic therapy, the patient became septic and succumbed to his illness ten days after his readmission.

DISCUSSION

Granulocytic sarcoma (chloroma or extramedullary myeloid tumour) is a localized mass of myeloid precursor cells occurring at extra-medullary sites, including the bones (especially subperiosteal regions), soft tissues, lymph nodes, gum, skin, intestine, testis, breast, lacrimal glands, paranasal sinuses, nasopharyngeal and orbital regions. Involvement of the large intestine rarely occurs.[1-3,6]

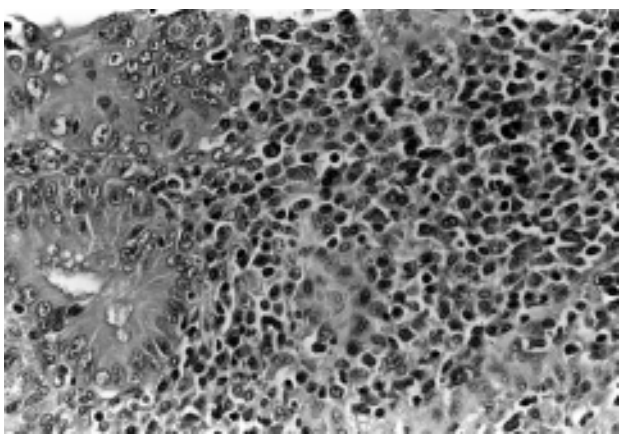

Figure 1. Presence of malignant myeloid cells within the stroma of well-differentiated carcinomatous blasts. (Haematoxylin-eosin, original magnification x400).

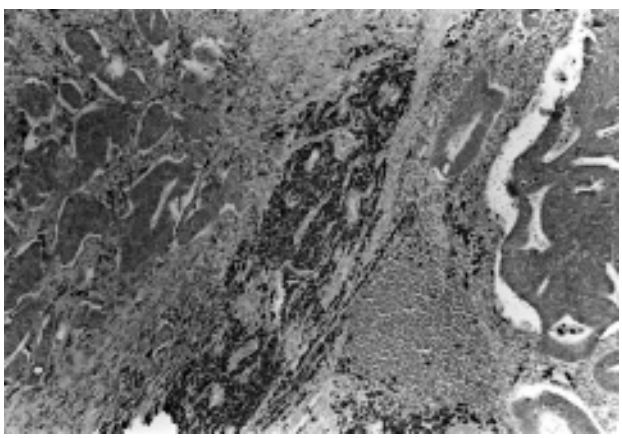

Figure 2. Malignant myetoid cells' immunoreactivity for myeloperoxidase (centre). Note the coexistence of cancer elements (ABC-horseradish peroxidase, original magnification x250).

It has no age preference[1] and may present in patients with AML, myeloproliferative disorders, other haematologic diseases, or in approximately 30% of cases without any known haematological disease.[2,6-8] The majority of the latter though, may eventually develop leukaemia.[1,6,8] Attempts at histopathological classification of granulocytic sarcoma have generally indicated three levels of differentiation: blastic, immature and differentiated. Today, no definite criteria for the classification of tumourous myelogenous proliferates exist.

Granulocytic sarcoma presenting in the absence of haematological disease is often misdiagnosed. Misdiagnosis may reach a 75% of unsuspected cases, resulting to incorrect treatment thus effecting prognosis.[2,3,6,8] The tumours most commonly confused with granulocytic sarcoma include non-Hodgkin lymphomas, Hodgkin' s disease, Ewing' s sarcoma and histiocytic lymphoma. Growth pattern and cell morphology may be helpful in differential diagnosis, as granulocytic sarcomas invade tissue with preservation of its architecture and cells have round to oval, reniform or many lobed nuclei, small nucleoli, a thin nuclear membrane and a delicate chromatin pattern.[7] The presence of eosinophilic myelocytes or metamyelocytes though extremely useful in recognizing granulocytic sarcomas may occur in only 50% of cases.[6] The description of cell morphology in granulocytic sarcoma is rather vague and lacks precision in that it neglects the spectrum of phaenotypic variability of this heterogenous tumour entity. Granulocytic sarcoma may be composed of myeloblasts or myeloid precursor cells with a tendency to differentiation into more mature neutrophilic and eosinophilic granulocytes. Taking into account the different degrees of cell maturation and differentiation, respectively, the correct diagnosis strongly depends on (immuno-) histochemical studies. Histochemical staining with NASD-CAE therefore, is useful in establishing the myeloid origin of the tumour cells, but may be focal, necessitating the use of immunohistochemical markers to confirm diagnosis.[2] Many have been proposed.[2,6,7] The use of a panel including MPO, lysozyme and CD43 with T- and B-cell markers has been suggested in recent literature.[2] Staining in the reported patient was positive for NASD-CAE, MPO, tysozyme, CD43 and CD68, the latter being a useful though nonspecific diagnostic marker[2] and negative for T- and B-cell markers. So, pathologic examination and immunohistochemistry confirmed the presence of a granulocytic sarcoma and an adenocarcinoma of the rectum. P53 immunohistochemical overexpression is regarded as a surrogate marker of genetic mutation, despite the fact that the antibody used reacts with both wild and mutant types of p53 proteins. In the examined sections, p53 was expressed in the vast majority of cancerous cells which thus seem to be genetically deficient, regarding the tumour-suppressor activity of the p53 gene. On the other hand, malignant haemopoetic cells were found to express this marker less intensely and at much lower percentages; therefore, the p53 functional status cannot be safely assessed by immunohistochemistry in this specific malignant subpopulation.

To the best of our knowledge, this coexistence has not so far been reported in the literature. The mechanism responsible for this rare combination probably is mere coincidence and so it appears likely that the fundamentally different tumour components arose from different mechanisms. However, specific genetic mutations occurring at gene loci with high proximity might hypothetically form the basis of this rare coexistence. Cytogenetic analyses of granulocytic sarcomas frequently involve chromosomal translocations that are typical of their disseminated counterparts. This aspect underscores the usefulness of morphological and immunochistochemical phaenotyping of granulocytic sarcoma. Interestingly, such analyses in previously reported granulocytic sarcomas have shown abnormalities involving chromosome 17[5], in which the p53 tumour-suppressor gene is also located; the latter gene is known to be implicated in development of colorectal cancer.[9]

Coexistence of granulocytic sarcoma with other solid tissue malignancies is extremely rare.[4,5] The rapid deterioration and the fatal outcome in the reported patient may have been associated to the combination of the two malignancies or the fact that MDS-related AML has a relatively worse prognosis.[10] Therapy of granulocytic sarcoma includes radiation, chemotherapy and possibly surgery. Aggressive combination chemotherapy at the time of diagnosis may improve prognosis and perhaps prevent the development of leukaemia[6] but the presence of infection excluded these options in the reported patient.

In conclusion, coexistence of rectal adenocarcinoma and granulocytic sarcoma though never reported before, should be recognized when occurring because prompt recognition of the latter is essential in order to commence proper therapy, thus improving prognosis.

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