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Granulocytic sarcoma: a diagnosis to be considered in unusual lymphoma syndromes

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Summary: A series of 7 patients with granulocytic sarcoma is presented to illustrate its varied clinical picture. In particular, this condition may present with features which suggest a non-Hodgkin lymphoma. The diagnosis will only be made if a high index of suspicion is maintained and special histopathological methods are used. Granulocytic sarcoma should be treated like an acute myeloid leukaemia.

Introduction

Granulocytic sarcoma (chloroma) is a rare extramedullary tumour composed of primitive cells of the granulocytic series. It was first described by Burns in 1811[1] and the name chloroma was used by King in 1853[2] to emphasize the greenish colour often found in the tumour which fades on exposure to air.

The tumour occurs in a variety of clinical settings and is often difficult to diagnose. It is closely associated with acute myeloid leukaemia which may be present at the time of initial diagnosis of granulocytic sarcoma, or, less commonly, may develop later.[3–6] When granulocytic sarcoma presents without evidence of acute antecedent or coexisting myeloid leukaemia the diagnosis may be overlooked.

The tumour is usually undifferentiated, making histological diagnosis difficult. However, certain techniques such as electron microscopy,[6] the chloroacetate esterase (CAE) stain and the immunohistological demonstration of lysozyme, an enzyme known to occur in the primary granules of monocytes and myeloid cells,[7] have been used to facilitate the diagnosis.

We describe 7 patients who have been seen at the Royal Marsden Hospital over the past 5 years. All of them presented diagnostic difficulty, and several were initially diagnosed as having non-Hodgkin lymphomas. They were only diagnosed by special histological methods or when acute myeloid leukaemia subsequently developed. We have not included patients presenting with acute myeloid leukaemia in whom soft tissue tumours (granulocytic sarcomas) were found incidentally and presented no diagnostic or management problems.

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Patients

The details of the 7 patients are summarized in Table I. Cases 3, 6 and 7 presented with syndromes clinically indistinguishable from non-Hodgkin lymphoma. Only one of the patients (case no. 7) had had a bone marrow examination done before attending the Royal Marsden Hospital and all of them had symptoms relating to their mass for between 2–7 months before the aspiration. In 3 cases (nos. 3, 4, 5) the finding of acute myeloid leukaemia prompted re-examination of the biopsy material with the use of the definitive CAE stain (Figure 1).

Although all the patients eventually died of their disease, patients who were treated with the regimens used for acute myeloid leukaemia had complete remissions lasting from 2–16 months (Table II). Those who were initially thought to have lymphomas and were treated as such did not have a period of remission.

Discussion

These cases illustrate the diverse presentations of granulocytic sarcoma and the extent to which they may mimic non-Hodgkin lymphoma. We cannot be certain that the outcome would have been better if all patients had been diagnosed immediately and treated with therapy appropriate for acute myeloid leukaemia. The survival of patients with granulocytic sarcoma is reported to be similar to that of patients with acute myeloid leukaemia in the absence of a tumour mass,[8] and various reports of granulocytic sarcoma preceding acute leukaemia suggest that it is of prognostic importance to recognize the condition and start systemic treatment with appropriate leukaemia

Table I Clinical, pathological and survival characteristics of patients

Patient no.	*Age (years) sex and race*	*Presenting syndrome*	*Initial histological diagnosis at RMH*	*Chloroacetate esterase stain on initial biopsy*	*Diagnosis of granulocytic sarcoma*
1	38 F African	L. submandibular and parasternal mass	Granulocytic sarcoma	Not done	AML on 1st marrow at RMH
2	53 M Pakistan	Mass R. upper arm and mass at porta hepatis	Granulocytic sarcoma	+	CAE
3	25 M Caucasian	Small bowel tumour causing obstruction	Poorly differentiated lymphocytic lymphoma	+	CAE and AML one month after diagnosis
4	38 M Caucasian	Bone pain with deposits in ribs	Anaplastic carcinoma	+	CAE and AML two months after diagnosis
5	8 M Arab	Bilateral orbital infiltration	Granulocytic sarcoma	+	CAE and AML on 1st marrow at RMH
6	26 M Iranian	Supraclavicular and axillary nodes Mediastinal mass	Diffuse histiocytic lymphoma	Not done	AML three months after diagnosis
7	33 M Caucasian	Flu-like illness L. supraclavicular nodes	Diffuse poorly differentiated lymphoma	—	AML 9 months after diagnosis

F = female M = male AML = acute myeloid leukaemia CAE = chloroacetate esterase
L = left R = right RMH = Royal Marsden Hospital

Table II Treatment and outcome

Patient no.	*First treatment*	*Initial outcome*	*Length of remission (months)*	*Subsequent treatment and outcome*		*(duration in months)*	*Survival presentation to death (months)*
1	BF9	CR	16	(1) BF9 + BMT	CR	17	40
				(2) E.C + DXR	CR	5	
2	BF9	CR	2	(1) DXR	CR	2	9
				(2) High dose M	Death		
3	BF9	CR	5	(1) BF9	CR	1	16
				(2) High dose C, E + BMT	CR	6	
				(3) MP, P	Death		
4	BF9	PR	Failed to attend for follow up				Unknown
5	CHOP one course Changed to BF9	CR	5	Bone marrow transplant	Death – Graft versus host disease		6
6	CHOP	PD	—	Multiple drugs	PD and death		3
7	CHOP	PD	—	Multiple drugs	PD and death		13

BF9
Adriamycin
Daunorubicin
Cytosine arabinoside
6-thioguanine
(an AML regimen)

CHOP
Vincristine
Prednisone
Cyclophosphamide
Adriamycin
(a lymphoma regimen)

C = Cyclophosphamide
E = Etoposide
M = Melphalan
MP = Mercaptopurine
P = Prednisone

BMT = Bone marrow transplant
CR = Complete remission
PR = Partial remission
PD = Progressive disease
DXR = Radiotherapy

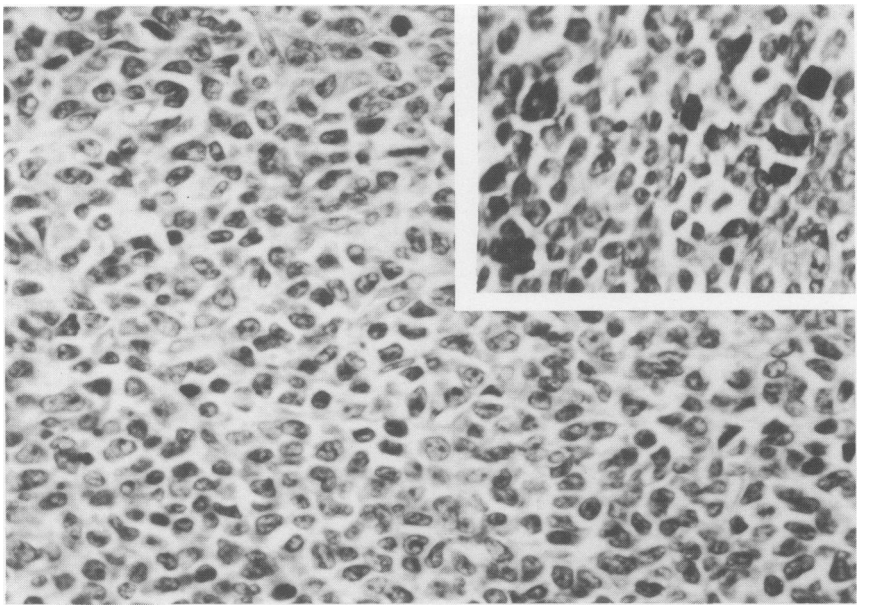

Figure 1 A lymph node replaced by granulocytic sarcoma. Normal structures are effaced by diffuse sheets of primitive myeloid cells with a high nucleocytoplasmic ratio and rather prominent nucleoli. There is no evidence of maturation in this example. The insert shows strong focal staining (black) of some primitive myeloid cells with chloroacetate esterase (CAE). Main illustration haematoxylin and eosin; both × 600.

regimens if survival is to be increased.[6,7,9,10]

The clinical and pathological diagnosis of granulocytic sarcoma continues to be a problem. It is essential to bear this condition in mind when confronted by problematic 'undifferentiated tumours' existing in soft tissues, bone or parenchymal organs. Bone marrow examination must be made and biopsy material stained with CAE. In addition, when doubt exists about the diagnosis of non-Hodgkin lymphoma – particularly in cases which behave atypically, such as failure to remit on conventional chemotherapy – then the biopsy material should be re-examined for CAE positivity.

If a granulocytic sarcoma is diagnosed in the absence of leukaemia we suggest that treatment with an acute myeloid leukaemia regimen should be used and consideration be given to bone marrow transplantation in remission.

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