

Case 2: Leukaemia Cutis

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CASE SUMMARY

History

A 70 year-old male patient presented with painless right cervical lymphadenopathy and progressive weight loss within three months. He was admitted into Prince of Wales Hospital for investigation. Lymph node biopsy was normal but blast cells (24%) were found in the peripheral blood smear. Bone marrow biopsy confirmed the diagnosis of Refractory Anaemia with Excessive Blast in transformation to leukaemia (RAEB-t).

He was later transferred to Pamela Youde

Nethersole Hospital for management of his hematological disease. A few weeks later, the patient complained of multiple, itchy brownish papules on the left axilla. The skin lesions gradually increased in number and spread to the trunk, neck and upper limbs. Each individual lesion became nodular and developed ulceration spontaneously. There was no history of vesicles. Dermatological opinion was given and a skin biopsy was performed. The patient was in good past health but he was diagnosed to have pulmonary tuberculosis during this admission. He was an ex-drinker and a non-smoker.

Examination

There was pallor but fever and generalized lymphadenopathy were not found. Cutaneous findings revealed multiple, brownish papulonecrotic nodules asymmetrically distributed over the neck, trunk and anterior chest; less densely distributed over the limbs (Figure 1). Skin lesions varied from 1.0 to 2.5 cm in diameter. In addition, asteatotic eczema was also found over both shins.



Figure 1: Multiple brownish papulonecrotic nodules on the trunk

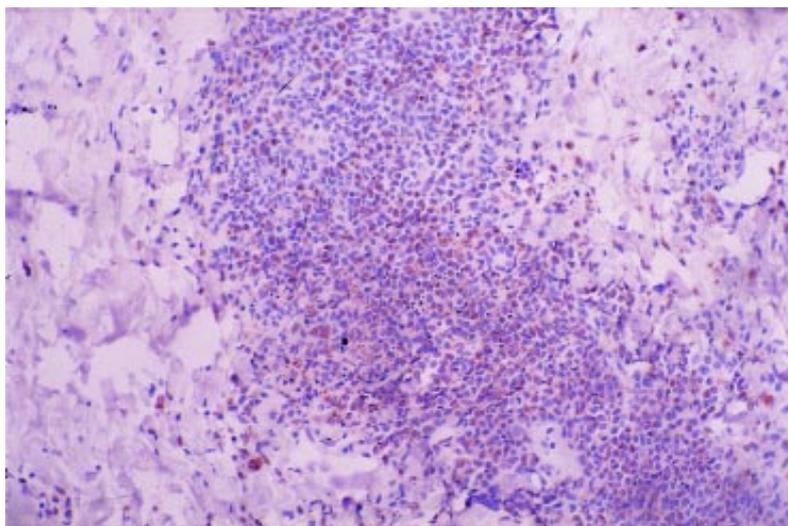


Figure 2: High power view showing monotonous population of atypical cells around blood vessels and skin appendages in the dermis. (By courtesy of Dr. N. C. Liou, SYPPI)

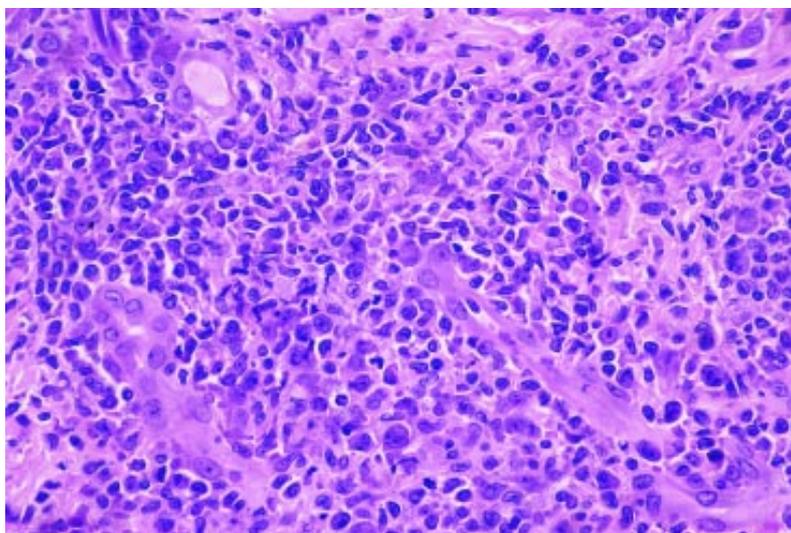


Figure 3: High power view showing positive staining of CD68 on atypical cells in the dermis, suggesting the diagnosis of Leukaemia Cutis of monocytic type. (By courtesy of Dr. J. K. C. Chan, Department of Pathology, QEH)

Investigations

Complete blood picture showed a low haemoglobin count (Hb: 8.2 g/dl), a high white cell count ($31.4/\text{cm}^3$) with 24 percent of blast cells and thrombocytosis (PLT: $704/\text{cm}^3$). Incisional skin biopsy for histopathology and immunophenotyping was performed on the back. A fairly monotonous population of abnormal cells with numerous mitosis were found around blood vessels and skin appendages in the dermis (Figure 2). These cells

were too atypical and too immature to be a reactive condition. The differential diagnoses included leukaemia cutis, skin metastasis and malignant melanoma. Special stains with S100 and cytokeratin (CAM5.2) were both negative, thus excluding the possibility of malignant melanoma and skin metastasis respectively. Immunostaining for myeloperoxidase was negative while CD68 stain was positive (Figure 3), thus suggesting the diagnosis of leukaemia cutis of monocytic but not granulocytic differentiation. In

correlation with clinical findings, the diagnosis was consistent with leukaemia cutis associated with RAEB-t.

Progress

In view of the patient's age, less aggressive treatment with oral hydroxyurea was given and the blast cells in peripheral blood were reduced to one percent. There was shrinkage of old leukaemia cutis lesions though new lesions appeared infrequently. In very refractory situation, electron-beam therapy might be considered. However the prognosis of this patient is very poor.

REVIEW ON LEUKAEMIA CUTIS

Leukaemia cutis (LC) is defined as skin infiltration by malignant hematopoietic cells. It usually occurs in the setting of marrow, peripheral blood and internal organ involvement. It is often regarded as a sign of dissemination of systemic disease or relapse of existing leukaemia. It is more commonly found in acute myeloblastic leukaemia (10% of total cases of LC) with a higher incidence in the myelomonocytic (M4) and monocytic (M5) subtypes.¹ Less commonly, it is found in patients with acute lymphocytic leukaemia, the overall incidence is one percent.

Clinical features

The clinical presentation of leukaemic cutis is highly variable. The common findings are small papules (2 to 5 mm), nodules or plaques. Less common features include ecchymoses, palpable purpura, ulcerative lesions, erythroderma, bullous lesions and gingival hypertrophy. Skin lesion may or may not be itchy. Its colour varies from pink, violaceous to brown, and sometimes it may have a hemorrhagic component. Rarely, it may appear green (chloroma) due to abundant myeloperoxidase-containing myeloblasts. Leukaemia cutis has been reported in scars from recent surgery, trauma, burns and herpes infection.^{2,3} The temporal relationship between LC and hematological malignancy also varies. It usually presents after or concurrent with the diagnosis of blood malignancy. There is a term called "aleukemic leukaemia cutis" that refers to the occurrence of skin lesions preceding blood manifestations and even bone marrow findings.

However, this term is a controversial issue because of the difference in the definition by different authors.

Leukemia cutis in association with myelodysplastic syndrome

Leukaemia cutis is less commonly associated with myelodysplastic syndromes. In a relative large series study of 40 patients with LC, there were 19 patients with myelodysplastic syndrome (MDS).⁴ Among the patients with MDS, LC preceded blood and/or bone marrow manifestations of leukaemia in nine patients (ranged from 3 weeks to 30 months), another seven patients developed skin lesions concomitantly with leukaemic transformation. This study showed that LC was an early manifestation of leukaemic transformation and the onset of LC might be important in identifying high-risk patients for early interventional therapy. In MDS, LC has a poor prognosis and death occurred in less than 3 months in 18 of 36 patients.⁵

Differential diagnosis

For a patient with haematological malignancy presenting with skin lesions, the differential diagnoses can be divided into two types: the specific and non-specific type. Specific skin lesion refers to leukaemia cutis that is not commonly encountered. The non-specific type is of utmost importance because of its higher incidence. This includes disseminated infection in immunocompromised host that can be caused by bacterial infection (*Staphylococcus aureus*, *Pseudomonas aeruginosa*), fungemia (*Candida*, *Aspergillus*) and viral infections (*Herpes simplex*, *Varicella-zoster virus*). Adverse cutaneous drug reactions, inflammatory disorders such as neutrophilic dermatosis (Sweet's syndrome, pyoderma gangrenosum), transfusion-associated graft-versus-host disease and vasculitis should also be considered in the list of differential diagnosis. An early skin biopsy for histology with request for immunophenotyping of atypical cells is highly recommended.

There are many different immunostains that are specific for certain cell groups. A list of the commonly used stains is shown in table 1.

Management

The success of treatment of leukaemia cutis is largely hindered by the associated hematological

Table 1. Commonly used immunostaining in dermatopathology

Marker	Specificity
1. Epithelial membrane antigen (EMA)	◆ Present in sebaceous glands, sweat glands and perineural fibroblasts
2. Carcinoembryonic antigen (CEA)	◆ Useful in the diagnosis of carcinoma especially metastasis
3. Leukocyte common antigen (CD45)	◆ Present in sweat glands and their tumors
4. S100-protein	◆ Present in haematopoietic cells
5. Chloroacetate esterase	◆ Specially useful in the distinction between lymphoma and poorly differentiated carcinoma
6. Myeloperoxidase	◆ Useful in the diagnosis of melanoma, neural tumors and histiocytosis
7. CD68	◆ Well differentiated granulocytes (mature stage)
8. CD3	◆ Poorly differentiated granulocytes (immature stage)
9. CD20	◆ Monocytes
10. CD4	◆ T-lymphocytes
	◆ B-lymphocytes
	◆ T-helper/inducer cells, macrophages

malignancy. Systemic chemotherapy which is adequate enough to induce and maintain bone marrow remission, usually fails to control cutaneous leukaemic infiltrates. Malignant cells surviving in the skin may then reseed the bone marrow, resulting in relapse. Electron-beam radiation therapy may eradicate skin disease but has no effect on bone marrow. Thus, the best results have been achieved with a combination of systemic chemotherapy and electron-beam radiation therapy.¹ PUVA and systemic chemotherapy is another option for some patients that are not suitable for electron-beam therapy.

Learning points:

There are many differential diagnoses in a leukaemic patient presenting with skin lesions. A skin biopsy with different immunohistochemical staining is invaluable to confirm the diagnosis of leukaemic cutis.

References

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