Langerhans cell sarcoma:
Case report of a diagnosis made in the Bone Marrow

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Introduction

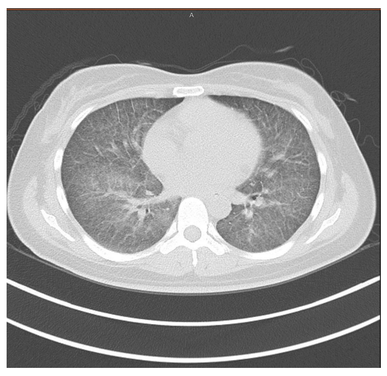
Langerhans cell sarcoma (LCS) is a rare histiocytic neoplasm derived from Langerhans cells that exhibits overt malignant behavior both clinically and pathologically. We herein report a case of LCS where the diagnosis was made on bone marrow examination.

Case Presentation

A 35-year-old Chinese woman with good past health presented with fever, cough and shortness of breath for 1 month.
Complete blood count showed mild anaemia:
Haemoglobin 10.5g/L WBC 5.63 x 10^9/L Plt 214 x 10^9/L
PET/CT imaging revealed hepatosplenomegaly, widespread lymphadenopathy, diffuse ground glass opacities in the lungs and diffuse marrow uptake along the spine.
Bone marrow aspiration and trephine biopsy were performed for further evaluation.

<u>CT images at diagnosis</u>
Figure 1a:
Ground class opacities in bilateral lungs

Figure 1b:
Gross hepatosplenomegaly



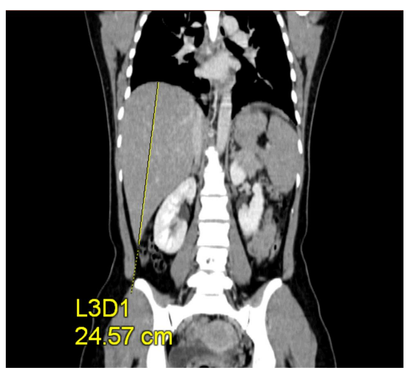


Figure 1a Figure 1b

Pathologic Features and Diagnosis

The bone marrow aspirate was aparticulate. Rare giant cells were seen amongst haematopoietic cells in the trails.
Bone marrow trephine biopsy showed prominent infiltration by medium to large sized abnormal mononuclear cells with pleomorphic appearance. They were positive for S100, and negative for common haematolymphoid markers CD45, CD3, CD20, myeloperoxidase, as well as cytokeratin marker (MNF116 and AE1/3). Further immunohistochemical stains were performed and the abnormal cells were positive for CD1a and Langerin, pointing to a Langerhans cell origin. Given the prominent cytological atypia, a diagnosis of Langerhans cell sarcoma was made. Sanger sequencing was negative for BRAF V600E. Subsequent para-aortic lymph node core biopsy revealed similar findings. Broncho-alveolar lavage also yielded isolated and loose aggregates of malignant cells.

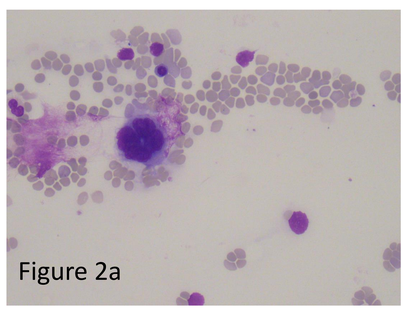
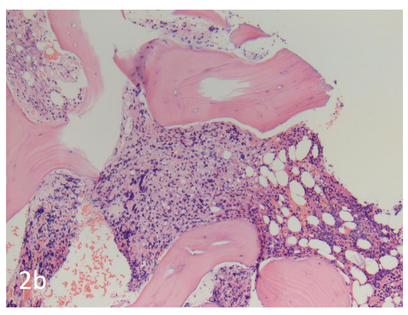


Figure 2a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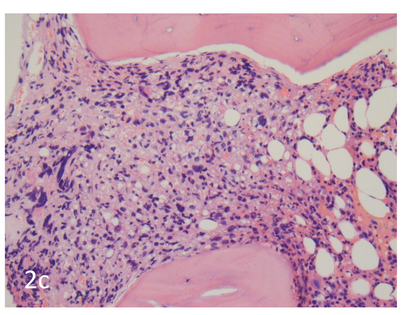
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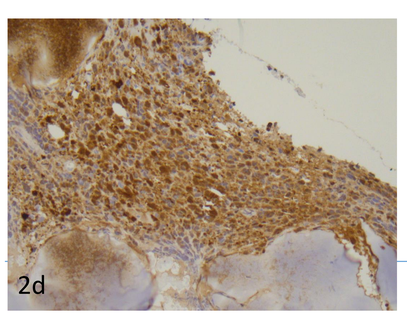
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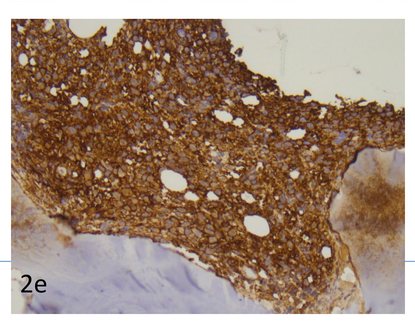
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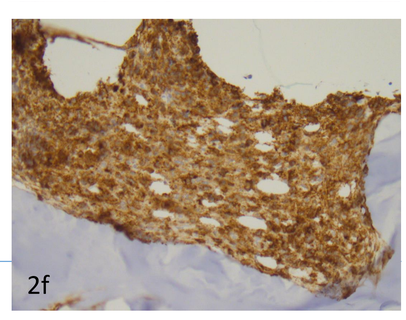
2f

Follow up

The patient treated with chemotherapy and attained partial response on PET/CT, while bone marrow biopsy showed residual disease involvement. She then underwent myeloablative matched sibling haematopoietic stem cell transplant (HSCT). Although occasional malignant cells were still found on the post-HSCT bone marrow biopsy, the patient remained clinically well 10 months post-HSCT.

Discussion and Conclusion

Langerhans cells are specialized dendritic cells resident in skin and mucosa that capture antigen for presentation and are capable of migration to lymph nodes. The WHO classification of Tumours of Haematopoietic and Lymphoid Tissues classifies tumours derived from Langerhans cells into two main subgroups according to the degree of cytological atypia and clinical aggressiveness: Langerhans cell histiocytosis (LCH) and Langerhans cell sarcoma (LCS).

LCS behaves more aggressively than LCH clinically. In a systematic review of 66 published cases of LCS, 27 (40.9%) had disseminated disease at presentation. Amongst these patients, lymph node (88.9%) was the commonest site of involvement, followed by skin (40.7%), liver and spleen (37%). Bone marrow involvement was reported in 6 cases. Median overall survival (OS) was 27.2 months for all reported cases, and only 6.3 months in disseminated cases.

In LCS, the tumour cells show characteristic Langerhans cell immunophenotype, being positive for CD1a, langerin (CD207) and S100. The distinguishing feature from LCH is in the morphology, with the tumour cells displaying an overtly malignant cytology, often with prominent pleomorphism such that they are not morphologically recognizable as Langerhans cells.

BRAF V600E mutations have been reported in approximately 50% of LCH. This mutation has also been sought in LCS and was found in at least two cases. However, in two other case reports involving 3 patients with LCS, BRAF mutation was not found.

Few cases of LCS are first diagnosed from bone marrow examination. Our case demonstrates the importance of appropriate immunohistochemical studies in the investigation of a malignant infiltrate in the bone marrow.

In summary, recognition of the characteristic Langerhans cell immunophenotype, together with the malignant cytology, are key to the diagnosis of LCS.

Figure 2a: Rare giant cell seen in bone marrow aspirate, Wright-Giemsa, 400x
Figure 2b: Bone marrow trephine biopsy, H&E, 100x. 2c: H&E, 200x. 2d: S100 stain, 200x. 2e: CD1a stain, 200x. 2f: Langerin stain, 200x

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