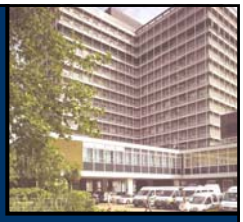
KRISTIN HENRY

IMPERIAL COLLEGE LONDON
at
CHARING CROSS HOSPITAL



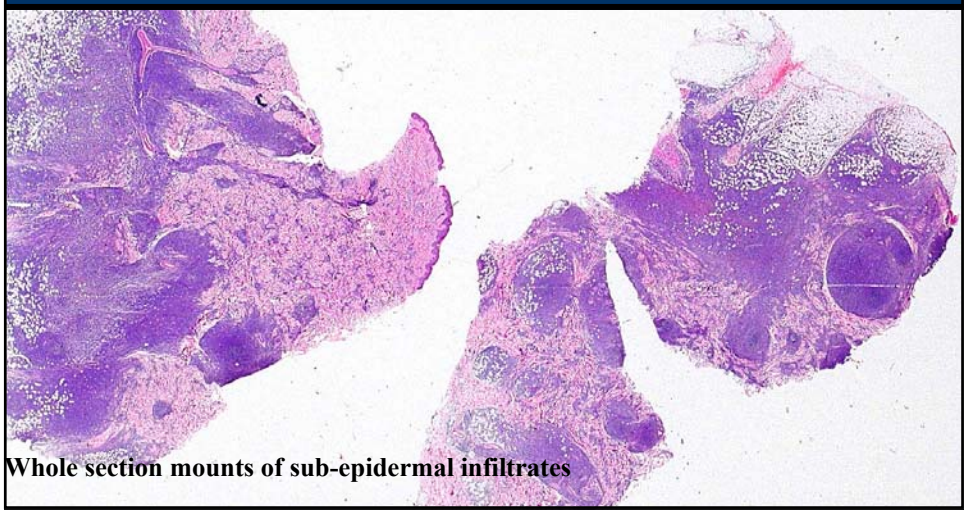
1st Scientific Meeting of the IAP Romanian Division

The Pathobiology and Molecular Biology of Tumours, Cluj, April 28-30 2010

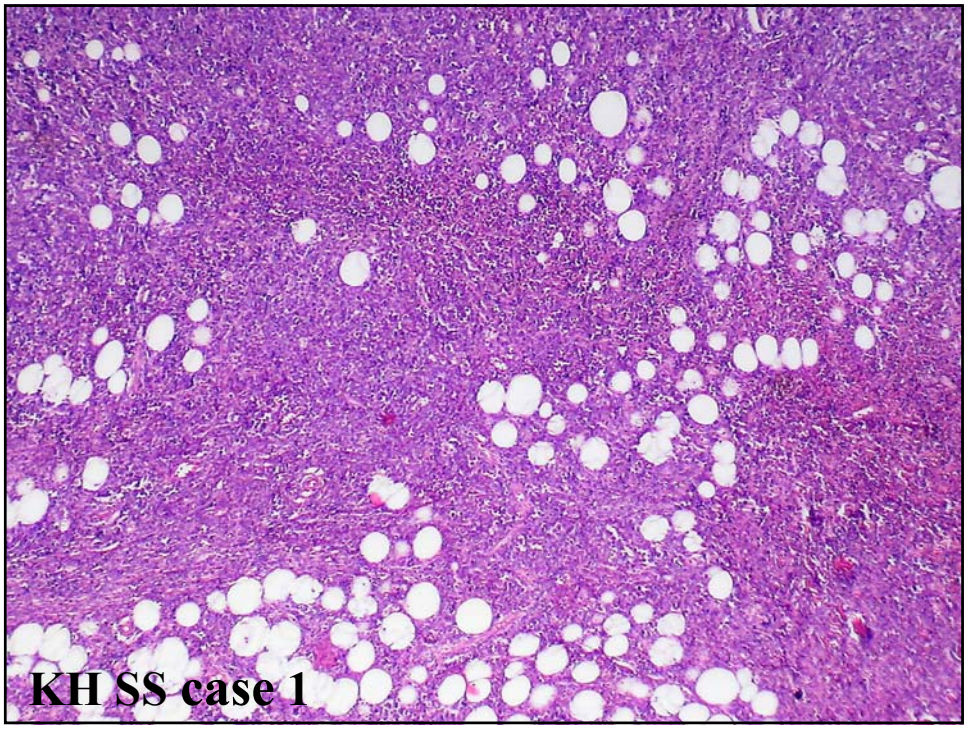
SLIDE SEMINAR: Haematopathology, Friday 30 April KH Cases 1 & 2

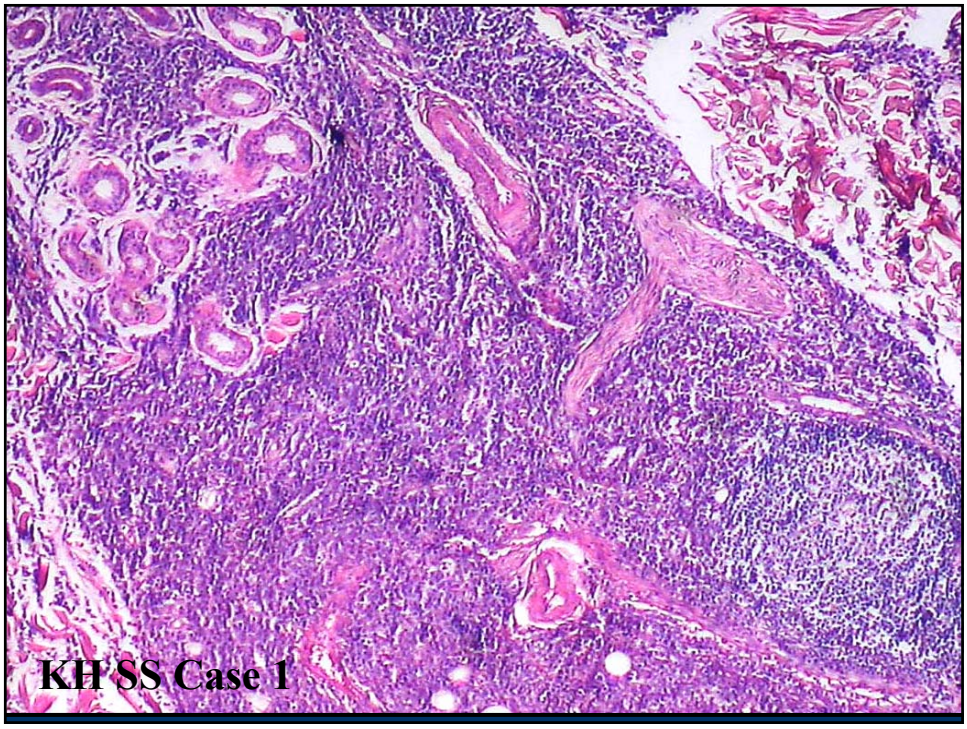
KH SS Case 1

Clinical data: man aged 32 years.
Developed 2 hard lumps in skin of upper arm initially diagnosed as insect bites. 2nd opinion saught. No other relevant findings.



Whole section mounts of sub-epidermal infiltrates


KH SS case 1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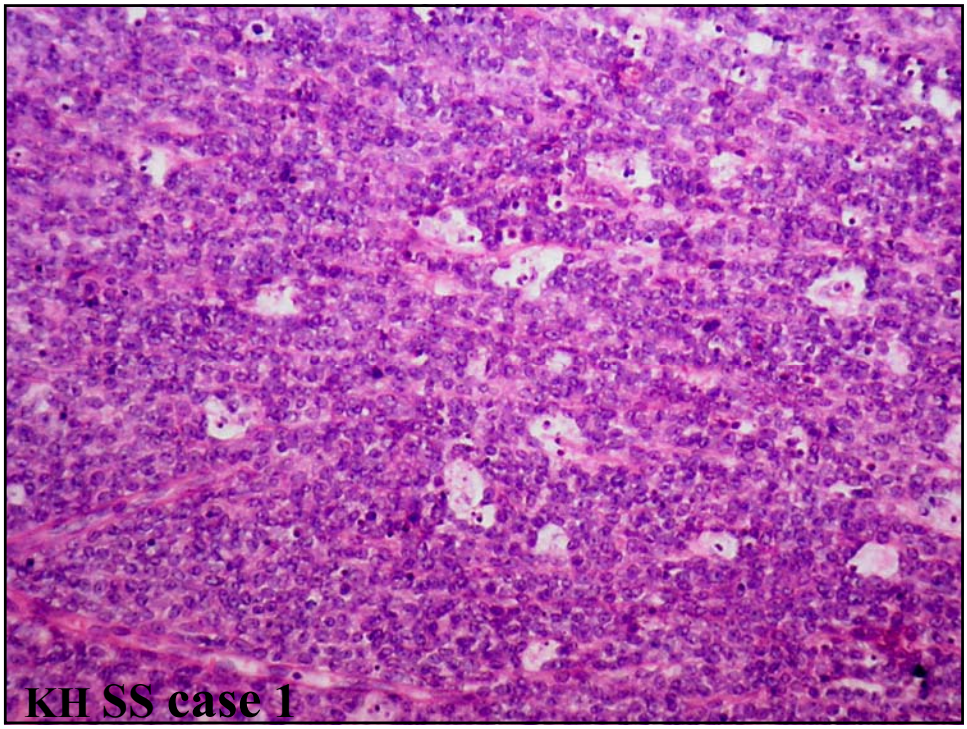
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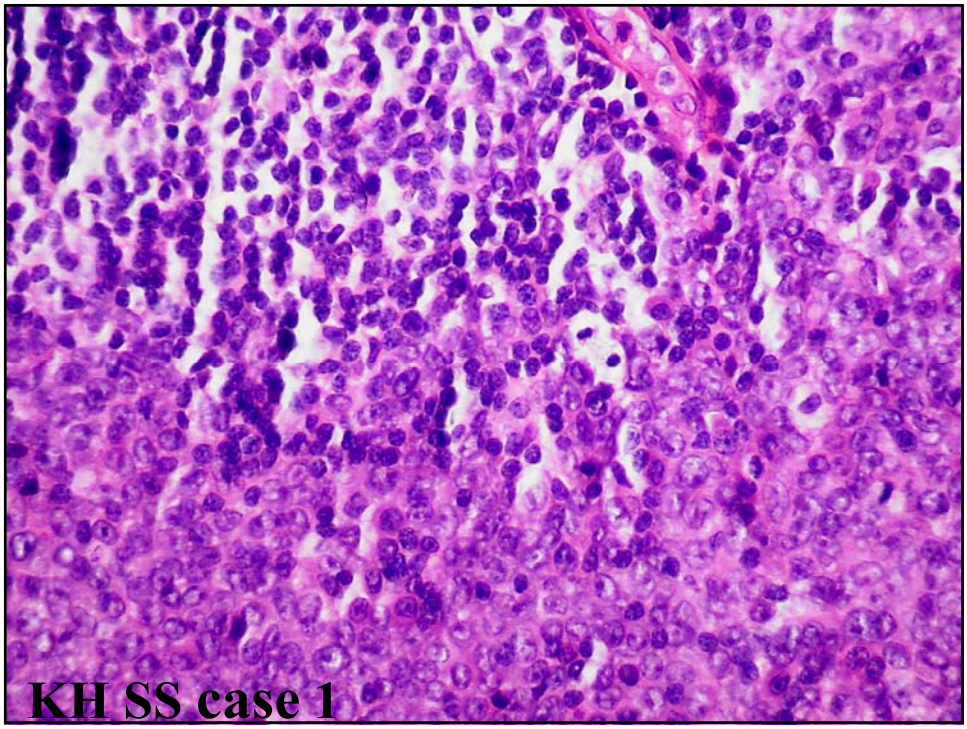
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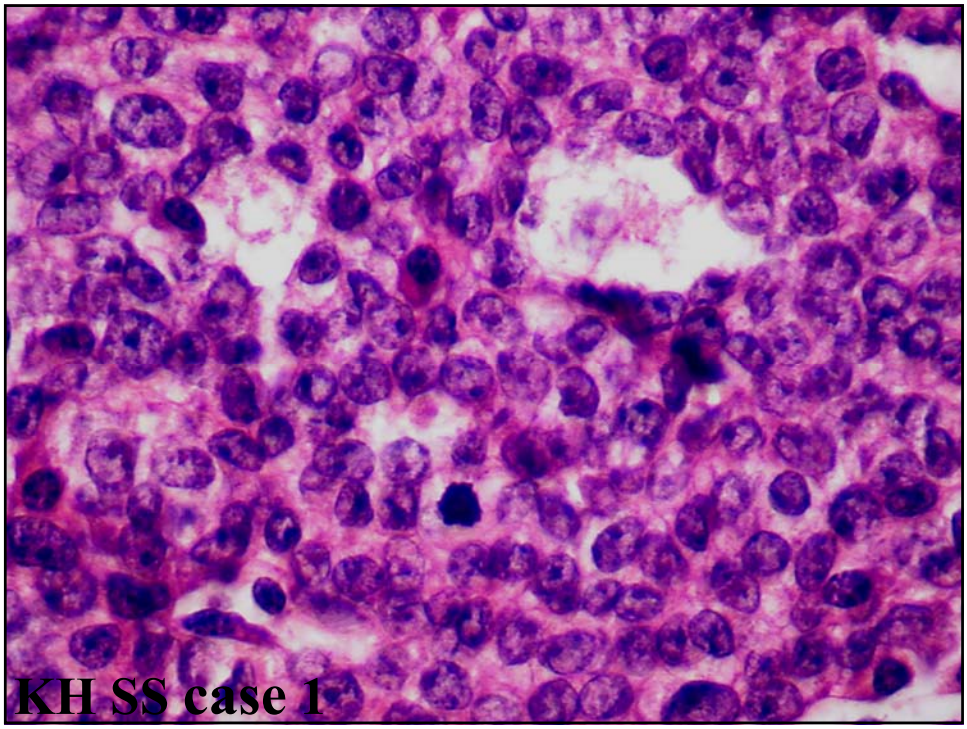
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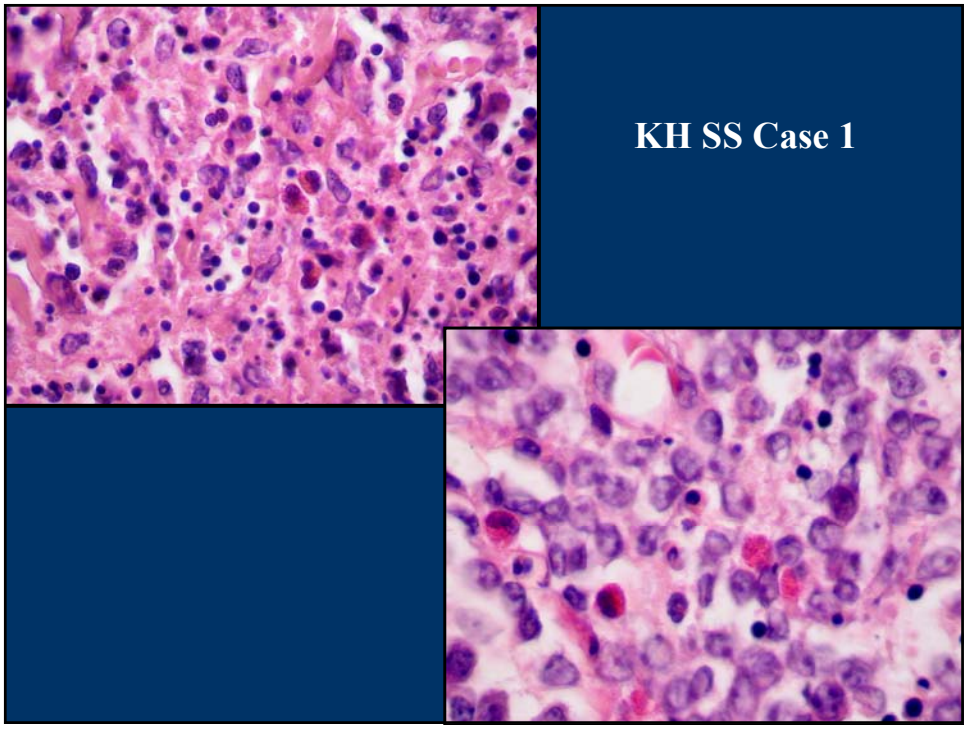

KH SS Case 1

KH CASE 1 HISTOLOGICAL FEATURES

Dermal infiltrate extending to sub-cutis. No involvement of overlying epidermis.

Residual lymphoid aggregates and occasional lymphoid follicles with GCs are surrounded by a monomorphous population of mononucleated cells.

In some areas there are large numbers of TBMs; these are associated with high apoptotic activity. A few foci of eosinophils are also present

The morphology of the cell is that of medium to large mitotically active blast cells with round nuclei, prominent nucleoli and little cytoplasm.

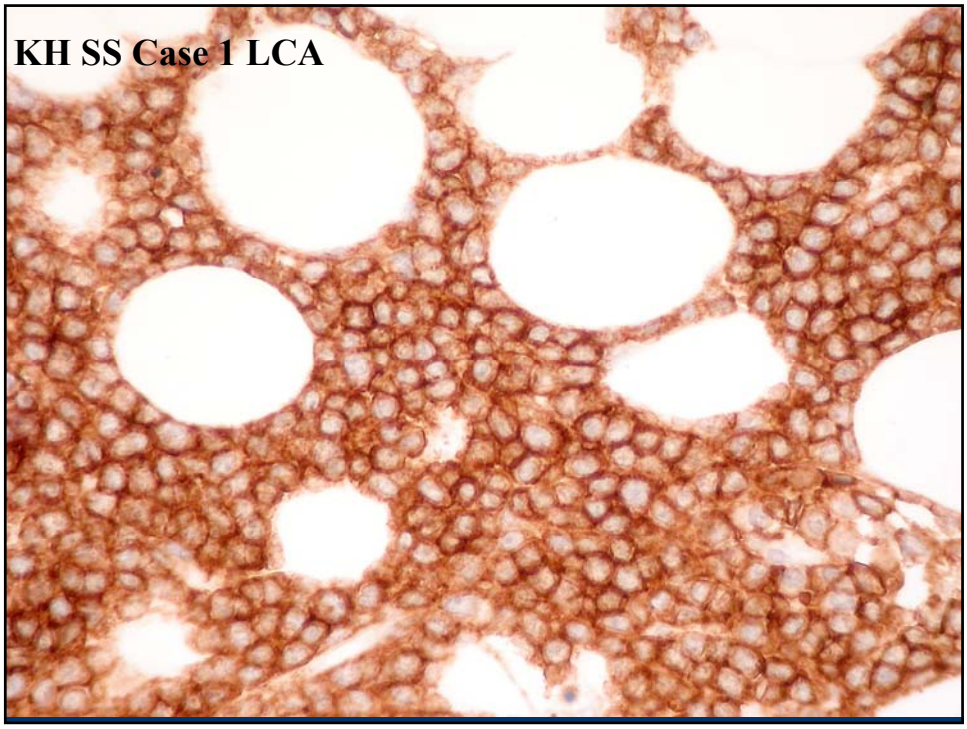
Case 1 DIFFERENTIAL DIAGNOSES

This lesion is obviously not an insect bite but a neoplastic infiltrate of monomorphic medium to large cells with high mitotic activity.

Differential diagnosis on routine staining:

NHL
Malignant melanoma (amelanotic)
Carcinoma
Other

KH SS Case 1 LCA



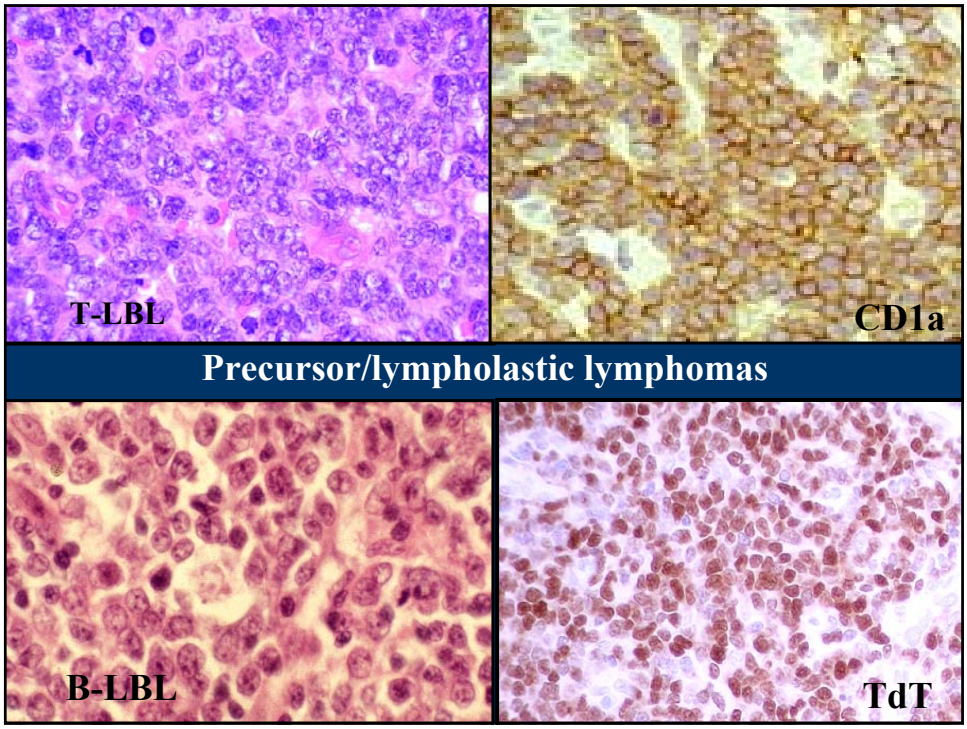
Case 1 DIFFERENTIAL DIAGNOSES

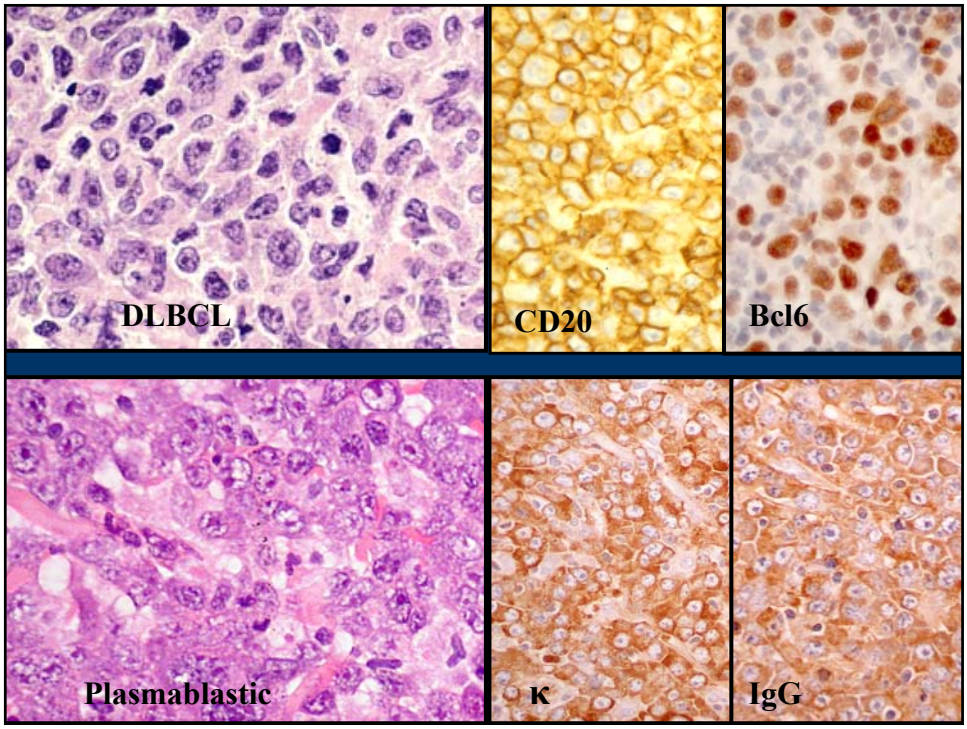
If lymphoma:

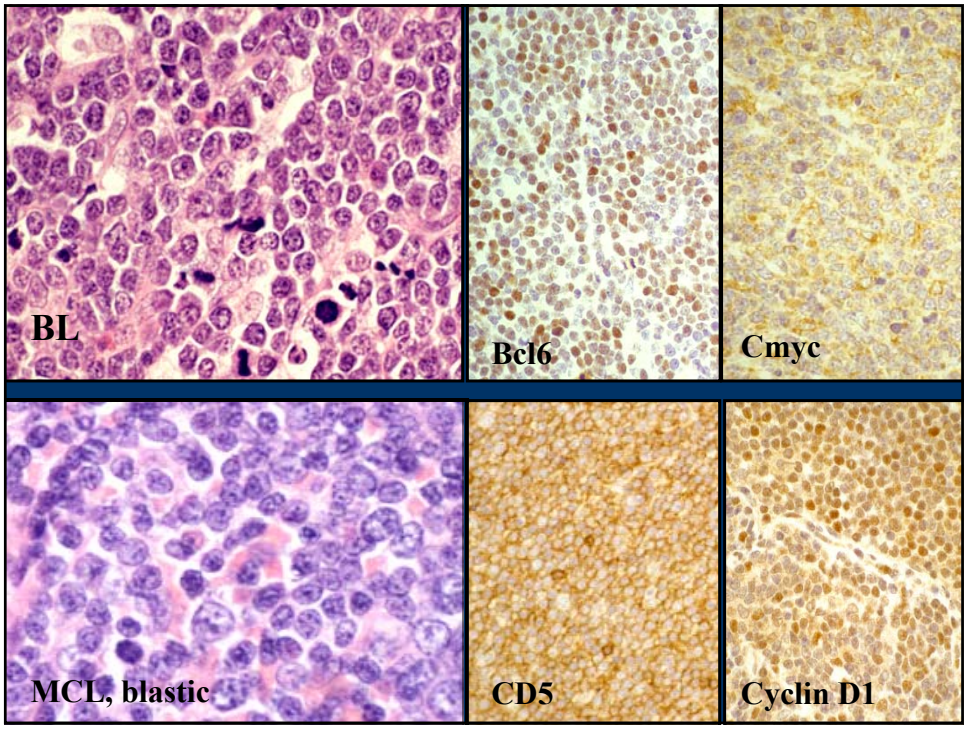
? BCL: B-ALL/LBL; DLBCL; BL; PBlL; blastic MCL
? TCL : T ALL/ LBL; ? TCL-nos; ALC

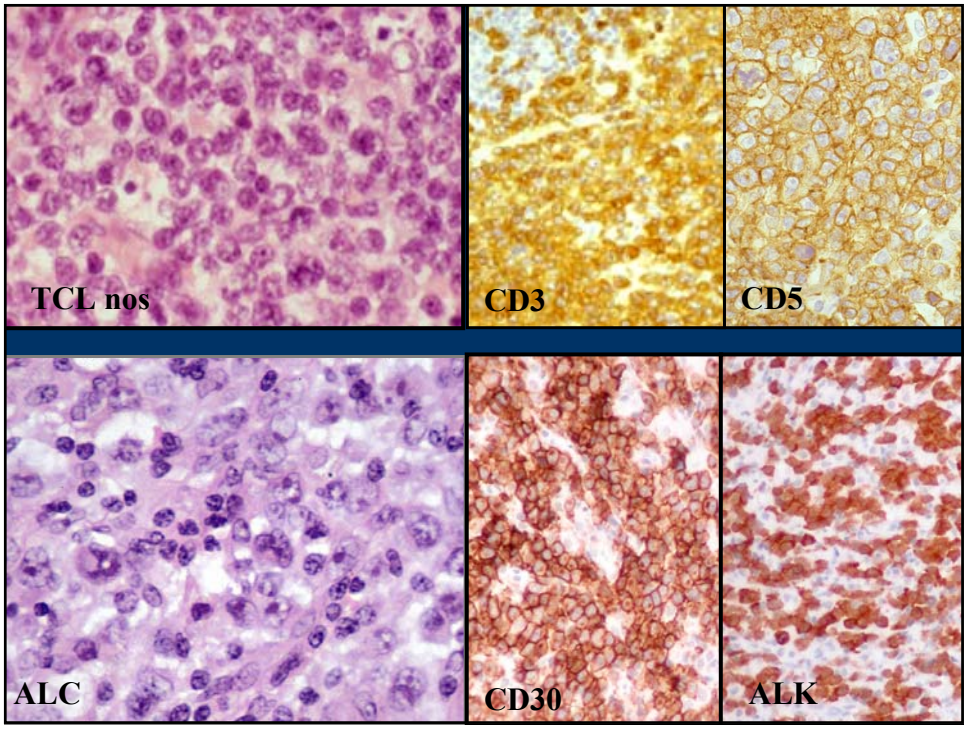
If other haematologic lineage:

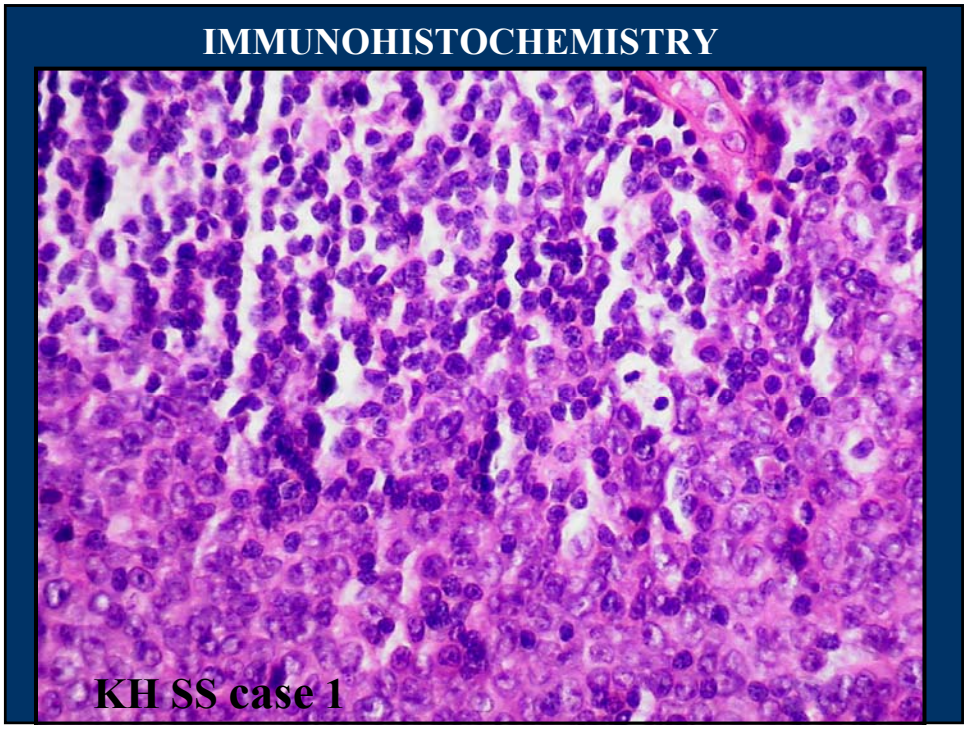
? histiocytic
? myeloid
? accessory/dendritic cell neoplasm
eg. blastic plasmacytoid dendritic cell neoplasm (CD4+CD56 +
haematodermic neoplasm; blastic N/K cell lymphoma)

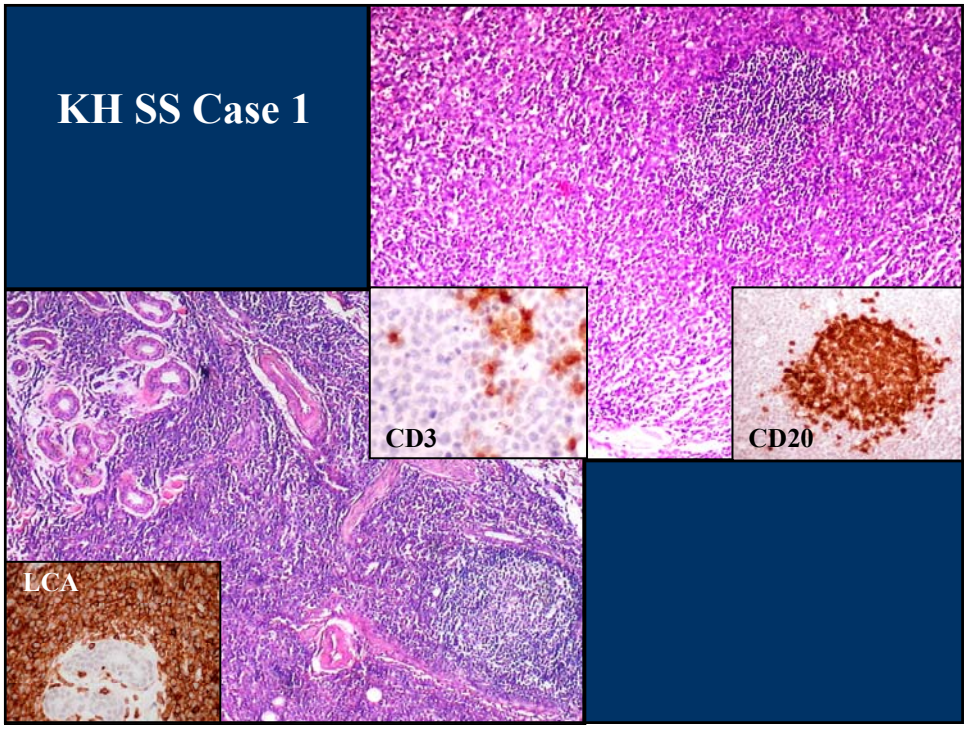

T-LBL
CD1a
Precursor/lympholastic lymphomas
B-LBL
TdT

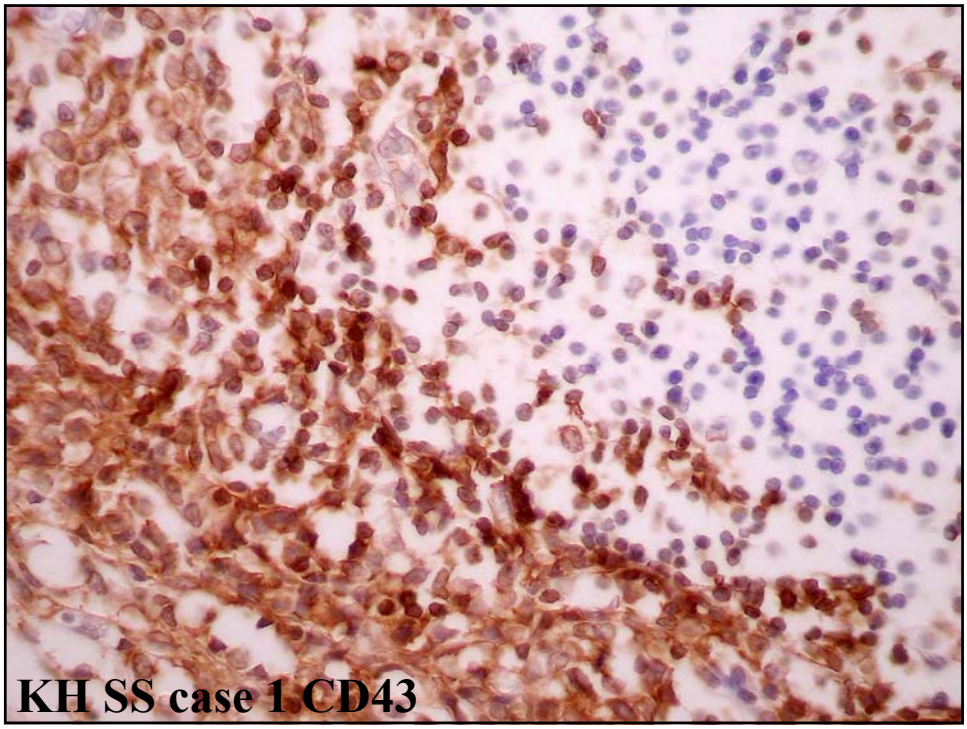

DLBCL
CD20
Bcl6
Plasmablastic
κ
IgG


BL
Bcl6
Cmyc
MCL, blastic
CD5
Cyclin D1

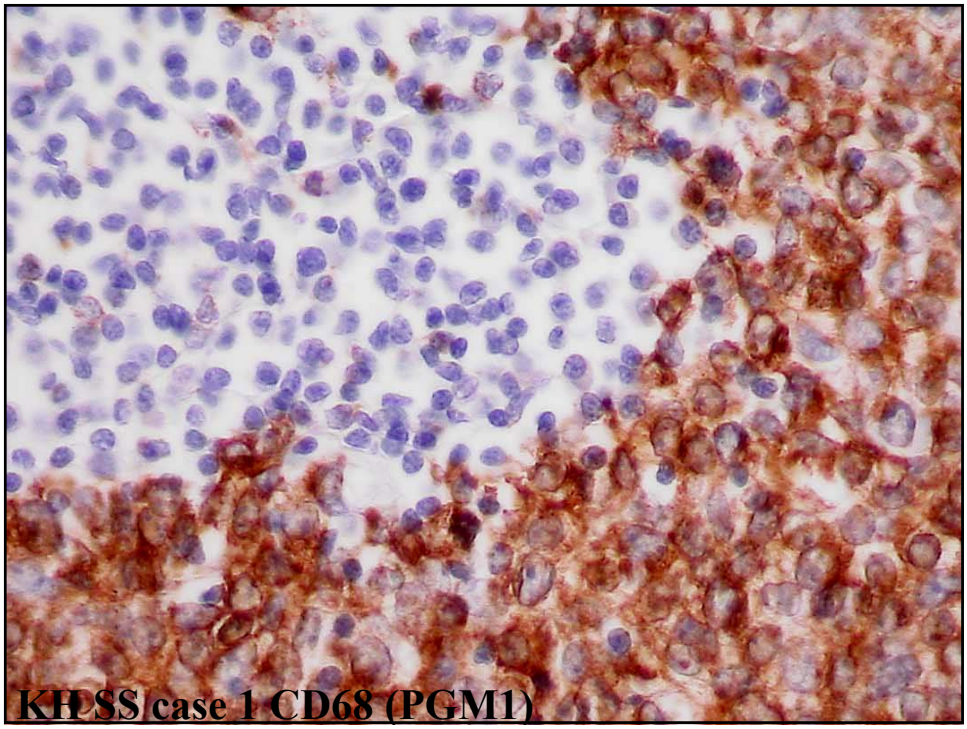

TCL nos
CD3
CD5
ALC
CD30
ALK


IMMUNOHISTOCHEMISTRY
KH SS case 1

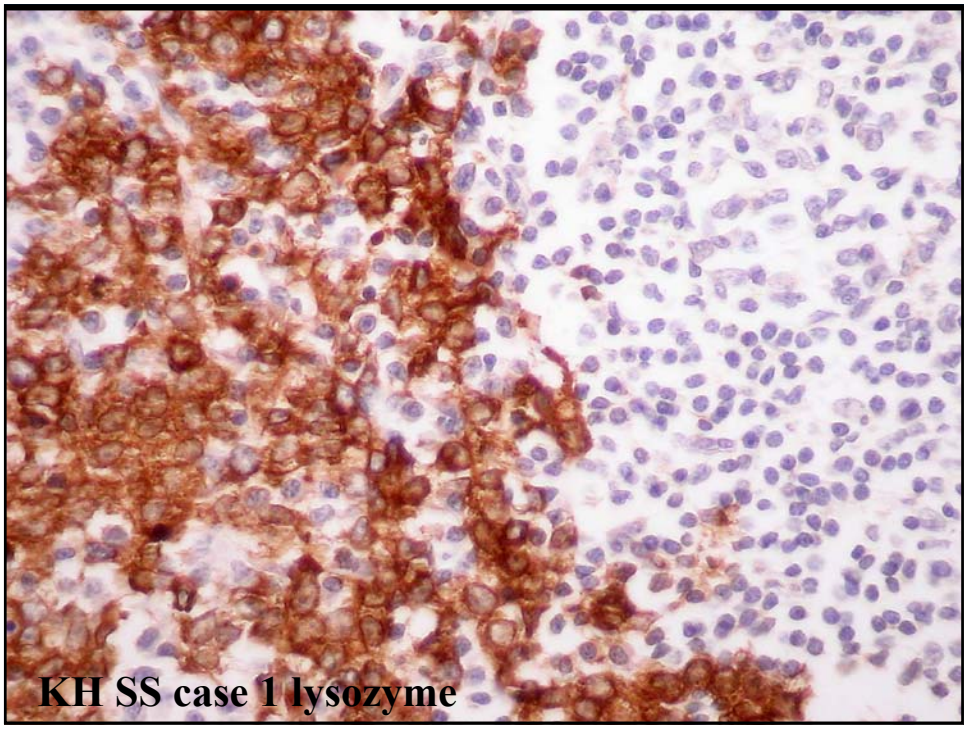

KH SS Case 1
CD3
CD20
LCA

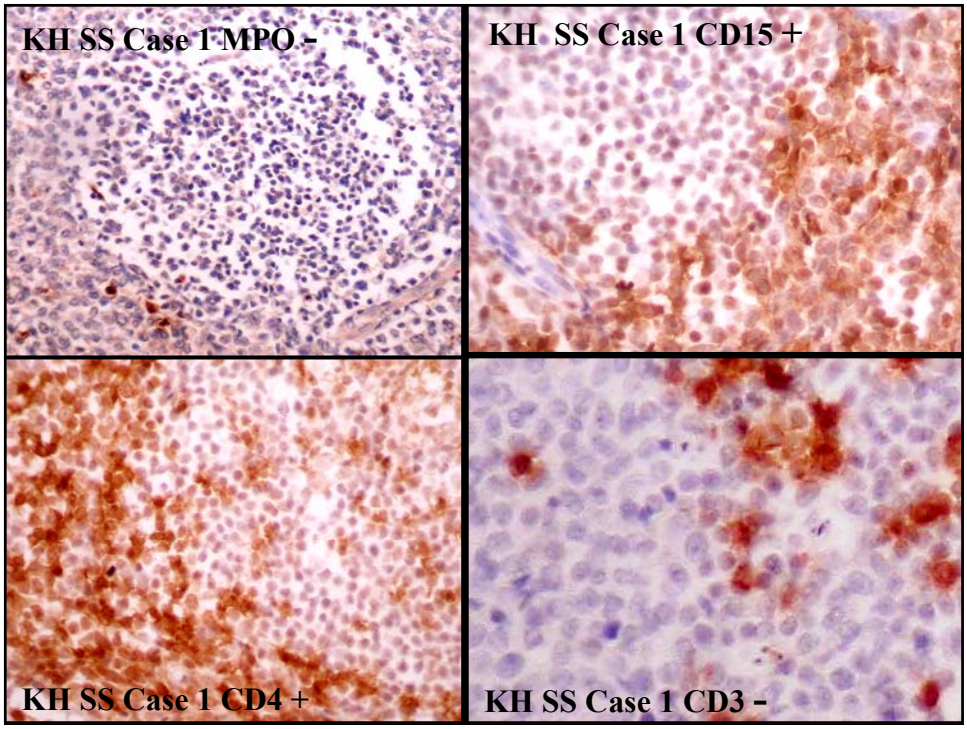


KH SS case 1 CD43



KH SS case 1 CD68 (PGM1)


KH SS case 1 lysozyme


KH SS Case 1 MPO -
KH SS Case 1 CD15 +
KH SS Case 1 CD4 +
KH SS Case 1 CD3 -

KH Case 1 Immunohistochemistry

LCA+, CD20-, CD79a-, CD3-, CD5-, CD43+, CD30-, ALK-
CD4 +, CD8-, Bcl6-, CD30-, CD34-, CD138-, MUM1-
TdT-, Granzyme B-, CD10-, CD56-, CD57-, CD117-
CD68 (PGM1)+, lysozyme+, CD15+, MPO+

CD21- FDC networks in residual follicles.
Ki67- PI 60-70%

Immunophenotype
CD43+, CD68 (PGM1)+, lysozyme+ CD15+, CD4+, MPO-, CD34-

KH Case 1

Man aged 32 years.
Developed 2 hard lumps in skin of upper arm initially diagnosed as insect bites.
2nd opinion sought. No other symptoms or relevant findings; PB and BM normal

Final diagnosis:
Myeloid sarcoma – *de novo*, monoblastic subtype

Immunophenotype:
LCA+, CD68 (PGM1)+, lysozyme +, CD 15+, CD43+, CD4+
CD3-, MPO-, CD34-, CD30-, CD56-, CD117-, TdT-

Comment: The morphology and LCA+ve expression prompted the diagnosis of lymphoma.
Without IHC, diagnosis not possible
The phenotypic profile CD4+/CD43 + but CD3- points to a myelomonocytic lineage tumour
Presentation before BM involvement, ie; *de novo*

MYELOID SARCOMA

- Tumour mass composed of myeloblasts or immature myeloid cells at many extramedullary sites
- Synonyms: granulocytic sarcoma, chloroma, extramedullary myeloid tumour
- Frequently misdiagnosed
- May be first evidence of AML or precede AML
- Majority consist of myeloblasts +/- features of promyelocytic or neutrophilic differentiation. Significant proportion myelomonocytic or monoblastic Trilineage or predominantly erythroid or MgK precursors rare.
- Most express CD43; a suspected lymphoma with the CD43+/ CD3- phenotype should raise suspicion of a neoplasm of myelomonocytic lineage
- Genetic abnormalities in about 55%: various Chr. abnormalities

Myeloid Sarcoma: Sites of involvement

- Subperiosreal bone*: skull, paranasal sinuses, sternum, ribs, vertebrae, pelvis
- Lymph nodes*
- Skin*
- Soft tissue*
- Mucosae: mouth, larynx, GI* & urinary tract
- Tonsil, spleen, thymus
- Various organs; eg, breast, gonads –testes* , kidney, lung, CNS
- Serosal cavities

* Most common sites

Myeloid sarcoma: Presentation

- Concurrent with acute myeloid leukeamia (AML)
- Precede the occurrence of AML by weeks, months or years – sometimes by many years
- Develop in patients with MDS or MPD heralding onset of blastic crisis
- As first manifestation of relapse in treated AML

Myeloid Sarcoma
Subtypes and Immunohistochemistry

Audouin J et al. Int J Sur Pathol. 2003

- Granulocytic variant: MPO +, CD68 (PGM1) -, lysozyme +, CD34+/-
- Monoblastic variant: MPO-, CD68 (PGM1) +, lysozyme +, CD34-
- Myelomonoblastic variant: MPO+/-,CD68 (PGM1)+/-, lysozyme+/-, CD34+/-
- Megakaryoblastic: Factor VIII+, CD31+, CD61+
- Erythroblastic variant: glycophorin C, blood group antigens

Myeloid sarcoma: clinico-pathologic, phenotypic and cytogenetic analysis of 92 adult patients

Pileri SA, Ascani S, Cox MC et al (2007) Leukemia 21; 340-50

Clinical data:

- Mean age 55.8 years
- Male-female ratio 1.42:1
- 27% de novo, 35% concurrent AML, 38% previous AML

Commonest sites:

- skin 28.2%), lymph nodes (16.3%), testis (6.5%), intestine, (6,5%), bone (3.25), CNS (3,25%)

Histology*:

- 50% blastic (n=46)
- 43.5% monoblastic(n=20) or myelomonocytic (n=20)
- 6.5% other subtypes (n=6)

* WHO criteria

Myeloid sarcoma: Genetics (WHO 2008)

Chromosomal aberrations 55%:

- monosomy 7
- trisomy 8
- MLL rearrangement
- Others- monosomy 16; 16q-; 5q-; 20q-; trisomy 3

16% NPM1 mutations

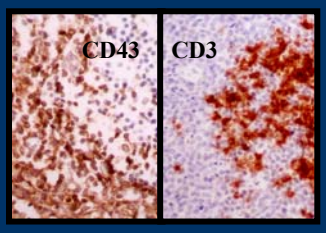
t(8;21)(q22;q22) of childhood MS cases less frequent in adults

MYELOID SARCOMA

With *de novo* presentation and if the tumour is myeloblastic
or
monoblastic without more differentiated myeloid cells present,
the diagnosis of MS is often missed or the tumour misdiagnosed

If lymphoma is suspected and IHC does not confirm diagnosis, this should lead to consideration of a non- lymphoid tumour.

Tumours with the CD43+/ CD3- phenotype should raise suspicion of a neoplasm of myelo-monocytic lineage

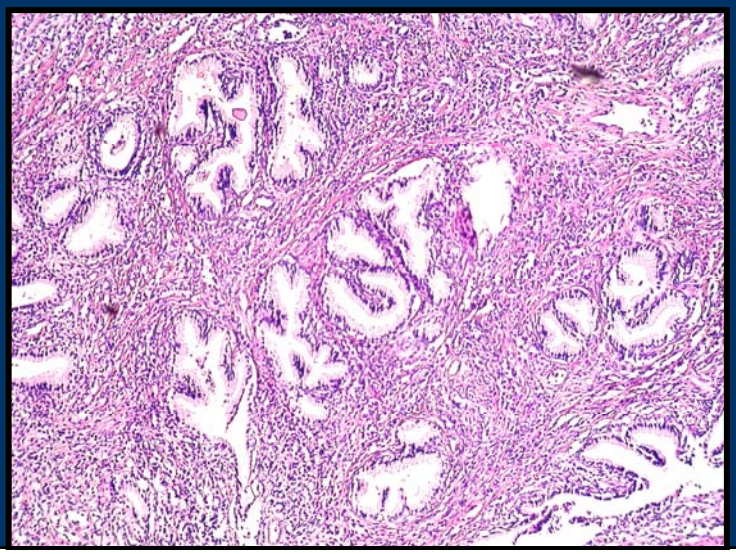


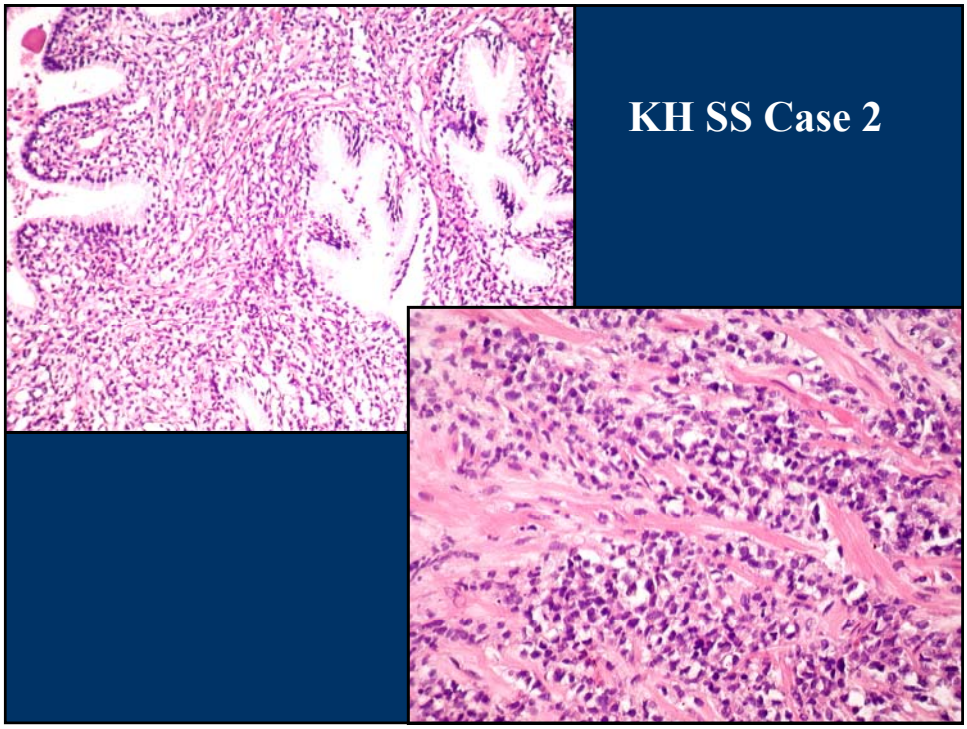
Treatment in *de novo* cases should be as for AML

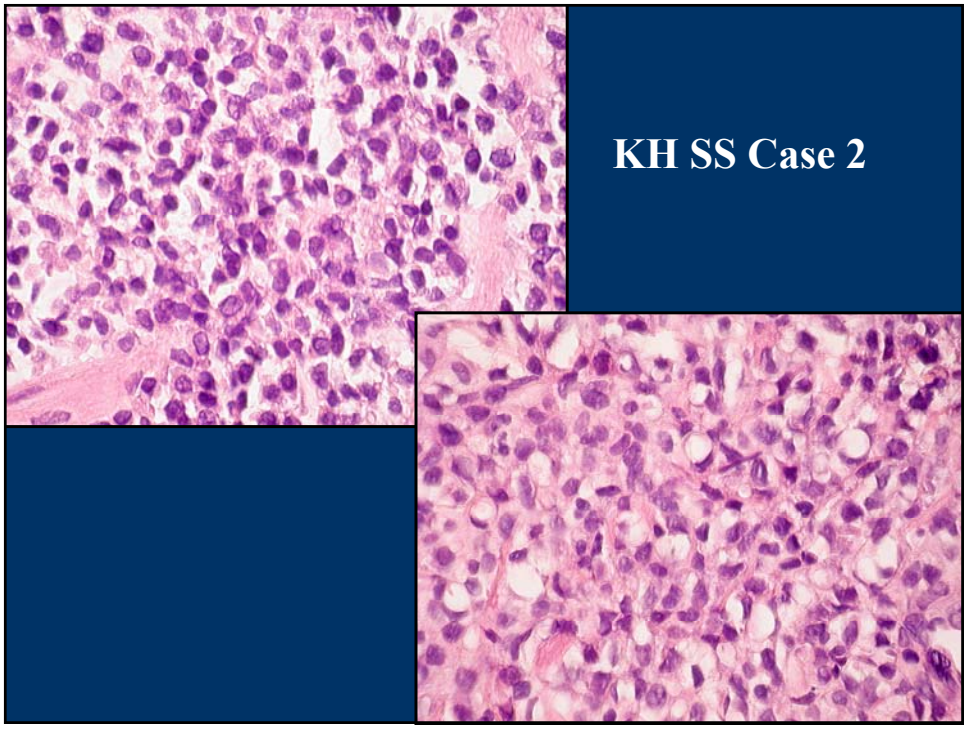
KH SS Case 2

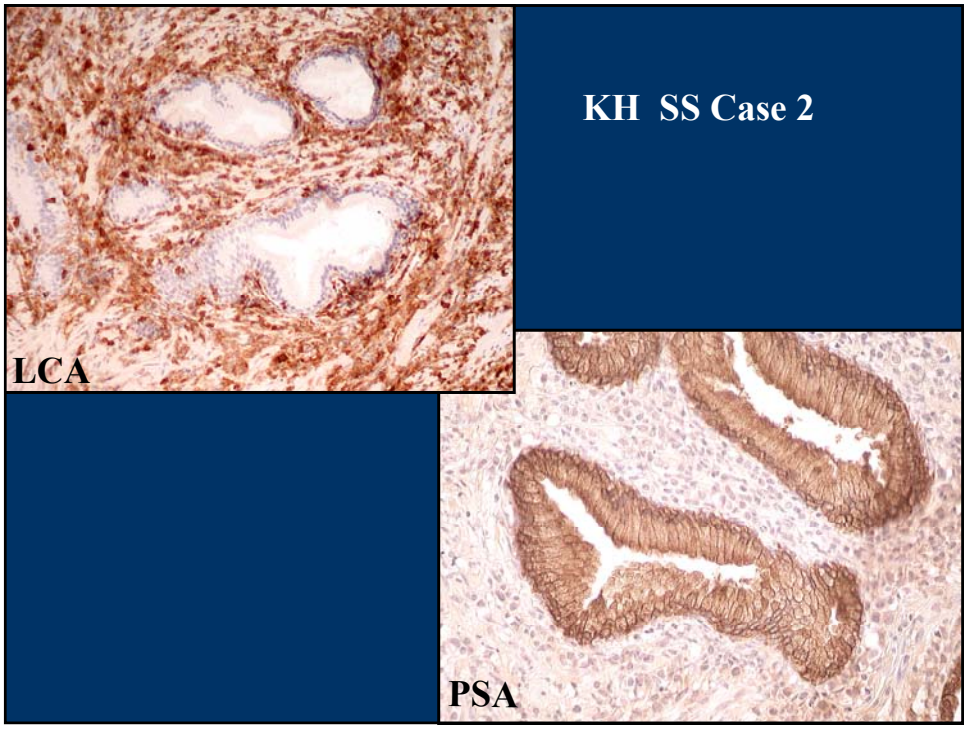
Man aged 73 yrs. Prostatic symptoms

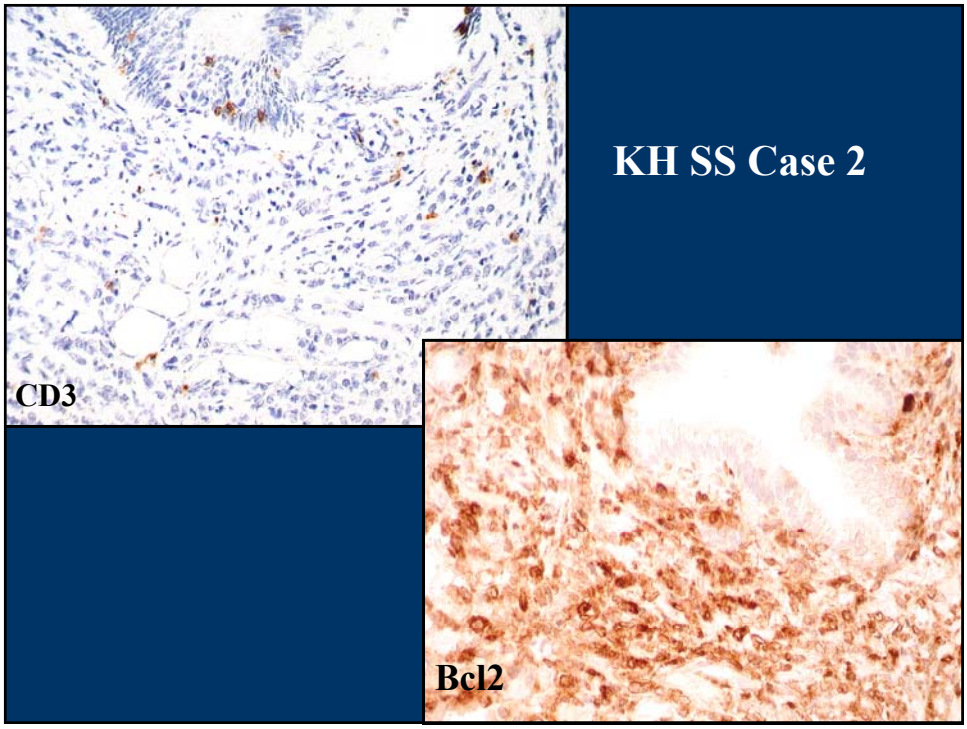
The prostatic biopsy showed a monomorphous cellular infiltrate.
? inflammatory; ? lymphoma; ? carcinoma

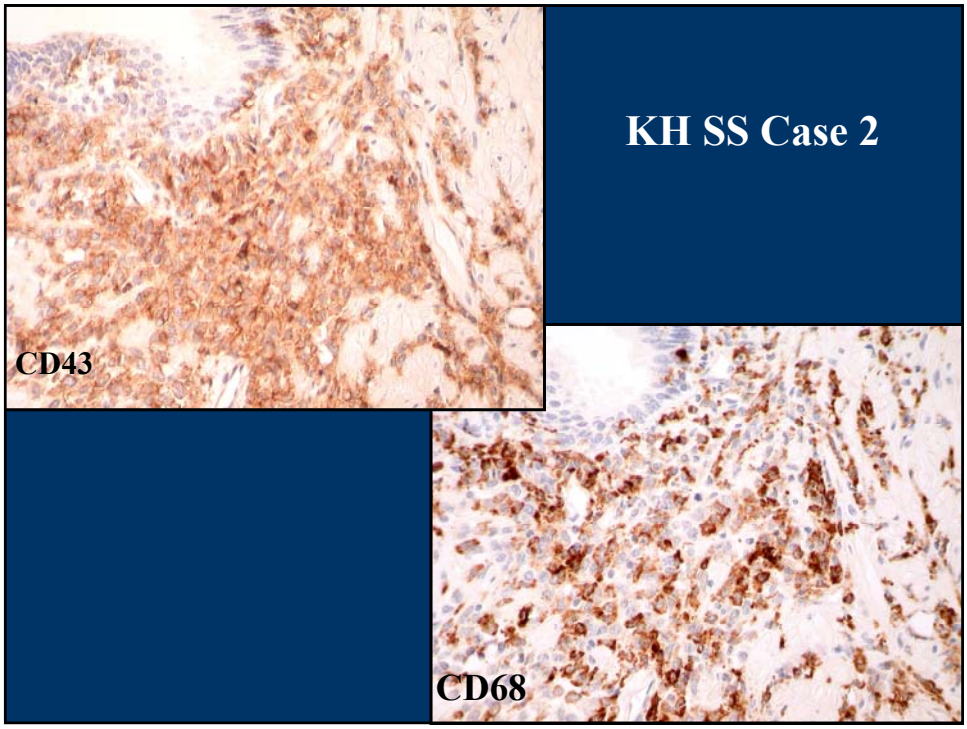



KH SS Case 2


KH SS Case 2


KH SS Case 2
LCA
PSA


KH SS Case 2
CD3
Bcl2



Case 2 Immunohistochemistry

LCA (CD45)+, PSA-, AE1/AE3-, Bcl2 +, CD3-, CD20-, S100-
CD43+, CD 68+

The CD3-/CD43+/CD68+ immunophenotype strongly suggested neoplasia of myelomonocytic lineage.

On giving verbal diagnosis of a neoplasm of myelomonocytic lineage and requesting additional sections for further IHC, information was given that patient had just been diagnosed with acute myeloid leukaemia (AML)

Case KH 2

Man aged 73 years.
TURPs showed a diffuse cellular stromal infiltrate ;?inflammatory, ?lymphoma, ?carcinoma
Case referred for opinion

Immunophenotype: **LCA (CD45)+, CD3-, Bcl2 +, CD43+, CD 68+**
No further sections available for sub-typing

FINAL DIAGNOSIS: AML infiltration of prostate

Comment: **The CD3-/CD43 +/ CD68 phenotype of the infiltrating cells pointed to a myelomonocytic lineage tumour**

Infiltrates by myeloblasts in leukaemic patients are not classified as myeloid sarcoma unless presenting a a tumour mass with effacement of architecture.