BCR-ABL1 positive Myeloid Sarcoma

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Cytocell UK & Ireland User Group Meeting
Jesus College, Cambridge
4th - 5th April 2017
Myeloid Sarcoma

WHO Classification Tumours of Haematopoietic and Lymphoid Tissue (2008):

‘Myeloid Sarcoma is a tumour mass consisting of myeloid blasts with or without maturation, occurring at an anatomical site other than the bone marrow.’

Can occur at almost any site in the body (skin, LN, GI, bone, soft tissue, testis)

Differential diagnosis: NHL, small round cell tumours (Ewings, rhabdo, NBL, medulloblastoma) undifferentiated carcinoma.
Myeloid Sarcoma

Can Occur:
Concurrently with BM disease (AML/MDS/MPN/CML)
As relapse of BM disease
De novo (may or may not go on to have AML in BM)

Cytogenetics:
-7, +8, KMT2A (11q23) rearrangements, inv(16)(p13q22) or t(16;16)(p13q22), +4, -16, 16q-, 5q-, 20q-, +11, t(8;21)(q22;q22) (paediatric cases), -5, complex karyotypes

Occasional reports in literature of BCR-ABL1 rearrangements.

Molecular:
~16% have evidence of NPM1 rearrangements (aberrant cytoplasmic NPM expression)
BCR-ABL1 Positive AML

Rare (<1% of AML Cases)

Difficult to distinguish between de novo AML and CML presenting in Blast Crisis.

The 2016 revision to the World Health Organization classification of Myeloid neoplasms and acute leukemia:

New provisional category of AML with BCR-ABL1

May benefit from TKI therapy.
Case Study

62 yr old Male

Presented in February 2015 with left leg pain and difficulty walking

CT imaging: Aggressive lesion in his left acetabulum

Needle Biopsy taken in April 2015

Histopathology conclusion: **Granulocytic Sarcoma (AML)**

Positive for CD45, CD34, CD117, CD33, CD99 and CD11c

Negative for lymphoma markers, plasma cell markers, carcinoma and melanoma
April 2015 – Referred to Barts

PET scan - large soft tissue mass around the left hip joint causing destruction of the acetabulum, ishium, left inferior pubic ramus and femoral head.

No other sites of disease on imaging.

Molecular studies (PB) –
   Negative for: JAK2 V517F,
   The most common CALR mutations
   MPL W515K/L mutations

Immunophenotyping (PB) – No abnormal population detected
Morphology:
Normocellular marrow with no morphological evidence of leukaemia

Immunophenotyping:
Approximately 2% of WBCs = CD34+/CD117+ myeloid progenitors

Trephine:
Short trephine.
One of three marrow spaces showed an increase in CD34+/CD117+ cells (15-20%).
No increase in blasts on morphological examination.
Correlation with flow/aspirate and clinical features required.
May 2015 - Bone marrow investigations

Cytogenetics:
- 47,XXY?c[12]

Molecular studies:
- No FLT3 ITD or TKD domain mutations
- No NPM1 mutations
July 2016 - Relapse

Presented at local hospital with diarrhoea, reduced mobility, confusion

Was hypercalcaemic, hypernatraemic and hypokalaemic

PB film - Pancytopaenic with circulating blasts

BM:
Morphology: **Relapsed AML**, 24% blasts.

Immunophenotyping: **Relapsed AML**
~28% of WBCs = myeloid progenitors

Trephine: **Diffuse infiltration by Acute Megakaryocytic Leukaemia (M7)**
Cytogenetics

48,XXYc,der(7)t(7;13)(p15;q12),+8,t(9;22)(q34;q11),-13, del(13)(q12q32),+19,+mar[cp12]

FISH confirmed the involvement of *BCR-ABL1* and showed the presence of a concomitant deletion of the *ABL1-BCR* sequences on the derivative chromosome 9.

Report Summary:
The t(9;22) is a rare but recognised finding in AML and is classified as an adverse risk cytogenetic abnormality according to the Revised MRC Prognostic Classification.
Example G-band karyotype
FISH – BCR/ABL1/ASS1
FISH on original Sarcoma biopsy
‘Current’ Clinical Information:

December 2016: Adverse reaction to chemotherapy (nausea, shingles, oral thrush)

Molecular (PB) – \textit{BCR-ABL1} transcript detected (Ratio = 0.779\%)

January 2017 (BM):
Morphology – Inadequate for morphology, suggestive of Residual Disease
Trephine – \textbf{Acute Myeloid Leukaemia (\textit{?M7}) with severe fibrosis}
PET – extensive disease in spine and long bones

Undergoing Palliative Care, possibly with additional chemotherapy. No further clinic letters.
FISH on diagnostic BM sample
Acknowledgements

Marianne Grantham
Amy Roe
Sally Walsh
Lorena Ripolles Tena
Camelia Andrei
Daniella Berneaga
Kate Gharibian
Bimpe Odewunmi
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