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PURE RED CELL APLASIA, IMMUNE THROMBOCYTOPENIA AND POST-TRANSFUSION COOMBS' TEST NEGATIVE HAEMOLYSIS DURING ANTI-PD1 THERAPY FOR METASTATIC LUNG ADENOCARCINOMA – CASE REPORT

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Anti-Programmed Death Ligand 1 (PD-L1) and Anti-Cytotoxic T-Lymphocyte-Associated Protein 4 (CTLA-4) checkpoint inhibitors are increasingly important treatment modalities for solid organ and haematological malignancies. Immune-mediated cytopenias are a rare consequence of checkpoint inhibition and include autoimmune haemolytic anaemia (AIHA), immune thrombocytopenia (ITP) and pure red cell aplasia (PRCA).

We report the case of a 75-year-old woman with metastatic lung adenocarcinoma on first line pembrolizumab therapy, presenting with profound anaemia with reticulocytopenia, moderate thrombocytopenia and haemolysis post red cell transfusion. Bone marrow biopsy showed absence of erythroid precursors, in keeping with PRCA, and presence of megakaryopoiesis, consistent with ITP. Extensive testing for the aetiology of haemolysis did not reveal a clear diagnosis.

She was treated with prednisolone initially, and red cell transfusion withheld. Due to inadequate response she was given intravenous immunoglobulin therapy which resulted in vigorous reticulocyte response and improvement in haemoglobin and platelet count. To date she has required no escalation of therapy.

In summary, we describe a rare case of concurrent PRCA and ITP during treatment with PD-L1 inhibitor therapy, and haemolysis of cryptic cause. Treating clinicians should be vigilant for the development of autoimmune haematological syndromes during checkpoint inhibitor therapy. Treatment with conventional immunosuppression is usually successful.

A RETROSPECTIVE ANALYSIS OF CORRELATION BETWEEN APTT AND ANTI-XA LEVELS USING EX VIVO PLASMA SAMPLES FROM PATIENTS ON INTRAVENOUS HEPARIN THERAPY

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Background: Intravenous heparin therapy is traditionally monitored according to activated partial thromboplastin time (APTT). Alternatively, monitoring by anti-Xa level testing may be less affected by pre-(analytical) variables. We analysed 105 samples from 46 patients who were on heparin infusions for concordance between APTT and anti-Xa levels. The existing

therapeutic ranges (TR) were defined as 60–100 s (APTT) and 0.3–0.7 U/mL (anti-Xa).

Results: Patients were predominantly male, admitted for treatment of acute coronary syndrome. Warfarin co-administration occurred in 20%. Median heparin rate was 100 U/h. Overall, 43% of samples showed concordance, with 21% of samples having both APTT and anti-Xa levels within the existing TR and 22% of samples having both APTT and anti-Xa levels in the sub-TR. In 19% of samples, the APTT was therapeutic whilst anti-Xa was sub-therapeutic. Variations in intrinsic pathway factors, fibrinogen or antithrombin were not predictive of discordance between APTT and anti-Xa.

Conclusion: Poor correlation between APTT and anti-Xa levels for monitoring heparin therapy cannot be explained by variations in other coagulation factors. Clinical outcomes correlation studies are required to determine optimal monitoring strategy for heparin therapy.

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RELAPSED/REFRACTORY ETP-ALL SUCCESSFULLY TREATED WITH NOVEL COMBINATION THERAPY VENETOCLAX WITH NELARABINE PRIOR TO ALLOGENEIC STEM CELL TRANSPLANT

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T lymphoblastic leukemia (T-ALL) is malignant neoplasm of immature T-cells that has characteristic immunophenotypic subtypes that correspond to T-cell maturation stages. Early T-cell precursor acute lymphoblastic leukaemia (ETP-ALL) is one such subtype, which is derived from thymic cells at the early T-cell precursor differentiation stage and make up 5–16% of T-ALL cases.¹ ETP cells are derived from haematopoietic stem cells that have recently migrated to the thymus, and retain multilineage pluripotency. They display reduced expression of T cell antigens; typically CD1a(–), CD5(–/dim) and CD8(–), and display aberrant expression of stem cell or myeloid antigens.² Congruently, the genetic mutations seen in ETP-ALL are similar to those found in poorly differentiated myeloid neoplasms.² ETP-ALL is historically thought to have a poor prognosis with standard chemotherapy, and a dismal prognosis in the setting of relapsed and refractory disease. Recent research has described how ETP-ALL is dependent on BCL2, and hence how antagonists such as ABT-199 (venetoclax) may offer a potential therapeutic benefit.³ This case study reports a patient with relapsed/refractory ETP-ALL with multiple genetic variants, who had an excellent response to a novel combination therapy of venetoclax with nelarabine prior to allogeneic stem cell transplant.

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VARIATION IN HAEMATOLOGY REPORTING – A DRAIN ON CLINICIAN TIME AND SOURCE OF CLINICIAN ERROR

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Aim: To review the variability in reporting formats of laboratory tests across Australian laboratories and assess the potential for resultant wasted clinician time and clinician interpretation errors.

Methods: Haematology reports (FBC, coagulation screen) were reviewed from 15 Australian laboratories (the majority in NSW) via convenience sampling. The formatting aspects of a total of 20 reports/views were reviewed for test name, sequence of results down or across page, units and reference intervals.

Results: There was wide variability across most formatting aspects. Six laboratories reported the most recent results at the left of the page and six on the right. There were 9 variations in FBC and 4 for coagulation screen test sequences down the page. There was variation in test names for the same tests e.g., 8 (slightly) different names for neutrophils. Multiple versions of reference intervals were observed e.g., 8 different reference intervals for white cell count and 10 for MCV. Different number of significant figures were used for reporting some tests.

Discussion: Improving the standardisation of laboratory reporting formats may reduce time expended by clinicians reviewing results and reduce the risk of clinician error when interpreting results. This can only be achieved by laboratories collaborating in standardising these factors.

HISTIOCYTIC SARCOMA TRANSFORMED FROM A LOW GRADE B LYMPHOPROLIFERATIVE DISORDER – A CASE REPORT

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Histiocytic sarcoma (HS) is a rare and aggressive lympho-hematopoietic malignancy that represents less than 1% of all non-Hodgkin lymphomas with poor response to therapy. According to the World Health Organization classification it is defined on the basis of morphological and immune-histochemical properties of mature tissue histiocytes.¹ It can occur sporadically or in association with other haematological neoplasms such as low-grade lymphomas (follicular lymphoma or chronic lymphocytic leukaemia among others).² Patients can present with either localised or disseminated disease involving organs such as the skin, central nervous system, spleen, gastrointestinal system, lymph nodes and the bone marrow. The pathogenesis of HS remains unclear and the presence of characteristic cytogenetic abnormalities such as PTEN, p14ARF and p16INK4A are currently non-contributory in the management or prognostication

of the disease.³ As a result of the rarity of the disease and lack of clinical trials, treatment strategies remain a challenge due to limited therapeutic options which are largely based on case studies. We report a case of a 65-year-old woman presenting with histiocytic sarcoma, transformed from a low-grade B lymphoproliferative disorder (LPD). This case aims to highlight the heterogeneity of this disease, aggressive course and the limited treatment options available.

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IDENTIFICATION OF TP53 ABERRATIONS IN CHRONIC LYMPHOCYTIC LEUKAEMIA USING DIFFERENT MOLECULAR DIAGNOSTIC TECHNIQUES

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TP53 aberrations arise through deletion or mutation of *TP53* gene. Accurate identification of *TP53* aberrations is important in risk stratification of chronic lymphocytic leukaemia (CLL).

Aim: To identify *TP53* aberrations in CLL using different diagnostic techniques.

Methods: Next-generation sequencing (NGS) for *TP53* mutation was performed in 104 CLL patients. Duplication/Deletion (Dup/Del) identification tool was developed in NGS analytic platform to identify *TP53* deletions. *TP53* deletions were also screened by fluorescent *in situ* hybridization (FISH) and multiplex ligation-dependent probe amplification (MLPA) in 81 and 40 patients respectively.

Results: *TP53* aberrations were identified in 29 patients; 27 had mutations with or without deleted *TP53* and 2 had sole *TP53* deletions. Of 43 mutations identified in these 27 patients, 26 mutations showed variant allele frequency of $\leq 12\%$. Most patients with mutated *TP53* (19/27) had no *TP53* deletions whereas 80% (8/10) of individuals with deleted *TP53* had concurrent mutations. Compared to FISH, sensitivities of Dup/Del tool and MLPA in identification of *TP53* deletions were 20% and 80% respectively.

Discussion: *TP53* mutation is the most frequent cause of gene inactivation. NGS should be offered to all CLL patients requiring treatment for proper prognostication. Regarding detection of *TP53* deletion, FISH is the best available screening technique.

METASTATIC MALE BREAST CANCER FOUND FROM BONE MARROW TREPINE

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