PB2047 MOLECULAR DIAGNOSIS OF CONGENITAL ERYTHROCYTOSIS IN A SINGLE HOSPITAL CENTER.

**Topic:** 16. Myeloproliferative neoplasms - Clinical

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**Background:**

The etiologic diagnosis of erythrocytosis is sometimes frustrating since about 70% are idiopathic. In primary erythrocytosis the only known form of congenital erythrocytosis is associated with erythropoietin receptor defects caused by mutations in the EPOR gene and has an autosomal dominant inheritance pattern. It is a rare entity that accounts for only 12% of erythrocytosis, with decreased EPO. Secondary congenital erythrocytosis present elevated EPO levels and normal erythroid precursors. They are mainly caused by mutations in genes of regulatory proteins of oxygen (O2) sensing pathways such as VHL, PHD2 (EGLN1) and HIF2A (EPAS1); mutations in α- or β-chain globin genes (HBB, HBA2, HBA1), or by mutations causing 2,3-bisphosphoglycerate mutase (BPGM) deficiency with 2,3-BPG deficiency, all of them presenting an increased affinity of Hb for O2.

**Aims:** To identify idiopathic erythrocytosis under follow-up in the hematology department and to study possible hereditary causes by means of molecular studies in order to be able to subsequently carry out a family screening.

**Methods:** Retrospective descriptive study of 13 patients under follow-up in the hematology department of the Hospital Príncipe de Asturias. By reviewing the clinical history, the personal and family history were gathered, alongside laboratory values at the time of diagnosis and the diagnostic tests used to rule out secondary and primary causes such as polycythemia vera (abdominal ultrasound, chest X-ray, blood gas analysis with cooximetry, etc.). All patients were tested for hemoglobinopathies at the Hospital Clínico San Carlos using high-performance liquid chromatography, capillary electrophoresis and DNA analysis. On the other hand, the Hospital 12 de Octubre performed a genetic study by next-generation sequencing (NGS), and the demographic and analytical characteristics are shown in the table.

**Results:**

From a total of 13 patients we have found a mutation causing erythrocytosis in 6 of them, among which there are two family clusters. The first group consists of three patients, two of them (father and son) with mutations in EPAS1 and TET2, and the third (uncle) in TET2 and DNMT3. The second familial cluster consists of a mother and her child with Syracuse Hb. There is one patient with mutation in the EPO receptor. Among the patients with no pathogenic alteration identified, we have found one patient with EPO above normal levels and two others with alterations in P50 in arterial blood gases (one with elevated P50 and the other decreased). In 80% of our patients, the therapeutic management has done been by means of periodic bleeding to obtain a hematocrit <45%, which has been interrupted on occasions due to secondary iron deficiency anemia. In 6 patients, who also had associated cardiovascular risk factors, antiplatelet treatment with salicylic acetic acid was associated with antiplatelet therapy (100 mg per day). None of our patients had thrombotic events or other incidences.

**Image:**
Summary/Conclusion:

The diagnosis of erythrocytosis is a challenge because the clinical features may overlap with different etiologies, and it is not possible to distinguish them by conventional biochemical and molecular techniques; sometimes these are pathologies with mild or even non-existent clinical features, which means a delay in the diagnosis of these patients. Since targeted NGS provides rapid and accurate mutation analysis, this technique could be applied directly to cases of erythrocytosis in which a genetic cause is suspected in order to improve patient and family counseling and initiate early treatment.