Introduction: Advancements in sequencing technology have dramatically improved our understanding of genetic kidney diseases such as polycystic kidney disease (PKD) and focal segmental glomerulosclerosis (FSGS). These tests have broad impacts on clinical care including prognostication, family planning, and transplant status; however, access remains difficult for many patients. Often the bottleneck to testing is the time to be seen by a member of the medical genetics team prior to testing. Our study used a multidisciplinary team of nephrologists, clinical geneticists, and genetic counselors to create a mainstreamed pathway to accelerate genetic testing for PKD and FSGS, and to determine if these pathways impact patient satisfaction and clinical care.

Methods: Mainstreamed pathways for genetic testing of patients with PKD and FSGS were developed and studied in a prospective cohort to assess time to return of genetic diagnosis and relevant clinical outcomes, and included survey data to assess patient perceptions. These pathways utilize gene panel testing, driven by patient phenotype. PKD patients received either a 2 or 8 gene panel, while FSGS patients receive a 45 gene panel. This was compared to a retrospective review of genetic testing under the standard system. We prospectively recruited 57 patients, 48 with PKD and 9 with FSGS, of which 35 have been consented to genetic testing through the mainstreamed pathway. 18 have had samples collected, and final genetic results have been returned to 11 patients with PKD and 3 with FSGS. Our retrospective control cohort who received the standard of care pathway contained 63 subjects, 56 with PKD and 7 with FSGS, with 58 having return of results data available.

Results: We successfully developed mainstreamed pathways for PKD and FSGS and have returned final genetic results to 11 patients within our publically funded healthcare system. The time from referral to return of genetic diagnosis in the mainstreamed prospective cohort was 114 days (95% Confidence Interval [CI]: 72-155 days), which is significantly shorter than the 387 days (95% CI: 328-446 days) in the retrospective control cohort (P<0.0001). In the 8 PKD patients we identified 3 positive variants in PKD1 and 1 in PKD2 giving a diagnostic rate of 50%, along with 4 variants of unknown significance (VUS) in PKD1. Within the FSGS cohort we have yet to identify a positive result given the low recruitment. Within the retrospective cohort of PKD patients, 29 of 56 had positive results in PKD1, PKD2, or GANAB with a diagnostic rate of 51% which was not different from the prospective cohort (P=1.0), with an additional 18 VUS identified.

Conclusions: The mainstreamed pathways led to a significantly faster time to return of genetic results compared to the standard system, and patients felt comfortable with these pathways. The panels used had diagnostic yields that were lower than expected in the PKD population and higher rates of VUS identification, but in line with our historic control. This may be due to the known difficulties in sequencing PKD1 due to its closely related pseudogenes.

No conflict of interest

POS-424

GENETIC ADMIXTURE OF U.S. HISPANICS FROM CENTRAL AMERICA

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Introduction: Chronic kidney disease of uncertain etiology (CKDu) has reached epidemic proportions in Central America in countries such as Nicaragua, Costa Rica, El Salvador and Guatemala, where it is a leading cause of premature death. CKDu mainly affects young male seasonal agricultural workers. There is some evidence for familial clustering of CKDu, with women and children also being tested, suggesting a genetic susceptibility. Understanding the ancestry admixture of affected populations can help to uncover their genetic risk to CKDu.

Methods: We compared the ancestry proportions from Africa, America and Europe of 1,075 Hispanics/Latinos enrolled in a US population-based study who also reported Central America country of origin of their four grandparents. We used genotypes from a genome-wide array and reference samples from the Human Genome Diversity Project, HapMap phase 3 and 1000 Genomes project Consortium to estimate European (EUR), West African (AFR) and Native American (NAM) ancestry at genomic locations. We summarized these estimates as global proportions of ancestry.

Results: The country of grandparent origin of participants was Guatemala (n=231), Honduras (n=296), El Salvador (n=104), Nicaragua (n=414), Costa Rica (n=22), Panama (n=8). Table 1 shows the descriptive characteristics and estimated ancestries of participants. Overall, the ancestry proportions varied by country of grandparent origin with higher NAM admixture among those from Guatemala and El Salvador, and a higher AFR ancestry proportion among those from Honduras. However, the NAM ancestry proportion was high in all groups from Central America.

Conclusions: This study is the first to compare the ancestry admixture of individuals from different countries in Central America. It provides important information on the genetic background of populations at risk of CKDu.

No conflict of interest

Table 1. Ancestry proportions by country of grandparent origin

<table>
<thead>
<tr>
<th>Country of grandparent origin</th>
<th>Guatemala (n=231)</th>
<th>Honduras (n=296)</th>
<th>El Salvador (n=104)</th>
<th>Nicaragua (n=413)</th>
<th>Costa Rica (n=22)</th>
<th>Panama (n=8)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (SD), years</td>
<td>47.8 (13.0)</td>
<td>41.1 (13.0)</td>
<td>44.0 (13.5)</td>
<td>45.3 (13.5)</td>
<td>52.3 (9.5)</td>
<td>47.0 (8.9)</td>
</tr>
<tr>
<td>% Males</td>
<td>46.3 (0.19)</td>
<td>39.2 (0.12)</td>
<td>40.4 (0.13)</td>
<td>37.4 (0.11)</td>
<td>31.8 (0.10)</td>
<td>0</td>
</tr>
<tr>
<td>Ancestry proportions</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AFR</td>
<td>0.07 (0.01)</td>
<td>0.21 (0.02)</td>
<td>0.09 (0.04)</td>
<td>0.12 (0.05)</td>
<td>0.06 (0.04)</td>
<td>0.33 (0.24)</td>
</tr>
<tr>
<td>EUR</td>
<td>0.40 (0.17)</td>
<td>0.40 (0.16)</td>
<td>0.39 (0.11)</td>
<td>0.44 (0.12)</td>
<td>0.63 (0.12)</td>
<td>0.38 (0.25)</td>
</tr>
<tr>
<td>NAM</td>
<td>0.53 (0.19)</td>
<td>0.38 (0.12)</td>
<td>0.52 (0.13)</td>
<td>0.44 (0.10)</td>
<td>0.31 (0.09)</td>
<td>0.29 (0.20)</td>
</tr>
</tbody>
</table>

POS-425

RECURRENT EPISODES OF FEVER IN A PATIENT WITH AUTOSOMAL DOMINANT POLycystic Kidney disease and Caroli Disease

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Introduction: Caroli’s disease (CD) is a very rare autosomal-recessive inherited disorder due to a saccular or fusiform dilatation and ectasia of the biliary ducts, it is often accompanied by cholelithiasis and subsequent cholangitis and frequently associated with congenital hepatic fibrosis (CHF).

The etiopathogenesis is still unclear but occasional familiar clustering suggests a possible hereditary disease, in particular when occurring in association with polycystic kidney disease and germline PKD1 gene mutations.

Methods: Here we describe a rare case of a 55 years old woman with a history of autosomal dominant polycystic kidney disease (ADPKD), autoimmune thrombocytopenia, Helicobacter Pylori infection and with recurrent episodes of fever of unknown origin often causing hospital admissions.

Results: During an episode of fever the patient underwent a Positron Emission Tomography (PET), which revealed an hypercapitation in hepatic hilum correspondence. Based on this finding, he underwent magnetic resonance cholangiography (MRC) that showed multiple cystic dilatations of bile ducts, ectasia of the common bile duct of 12 mm and also an anatomical variant of the biliary carrefour caused by a bifurcation of the branches of the right posterior bile duct. These morphological findings led to the diagnosis of CD (Figure 1,2).
Introduction: Wilson's disease (WD) is a genetic autosomal recessive disease, due to a mutation of the ATP7B gene, characterized by copper accumulation in the liver, eyes, and nerves. Renal involvement has been reported very rarely, affecting only 5% of WD cases. We present a case of WD associated with IgA nephropathy (IgAN).

Methods: Male patient with a diagnosis of WD established 11 years before the access at the Nephrology Unit. The patient initially presented with abdominal discomfort, undetectable serum ceruloplasmin levels, liver cirrhosis with an initial lenticular degeneration; the liver biopsy highlighted a hepatic copper concentration of 2930 mcg/g, also genetic investigations confirmed the diagnosis, with double heterozygosis for ATP7B gene. The patient started the therapy with copper chelators with a good clinical response through the years.

At the age of 21 he presented for proteinuria (1062 mg/24h) and hematuria, with renal function in the normal range (glomerular filtration rate 121 mL/min). IgA levels in the blood were slightly above the range (489 mg/dl).

Results: Renal biopsy showed mesangial cell proliferation, IgA deposition, and electron-dense deposit in the mesangial areas, all of which are consistent with IgAN and steroid therapy was started (Figure 1, 2, 3). Figure 1. Figure 2. Figure 3. The occurrence of two rare disorders is a very uncommon event. Both diseases have a similar incidence rate with about 1 case per 30,000 live births. In literature 3 clinical cases of WD associated with IgAN have been reported. Two were reported in children and one case occurred in an adult patient. However, in the previous adult case both diseases were diagnosed contemporary and WD treatment with trientine hydrochloride and zinc acetate caused a decrease in the serum level of IgA levels after initiating chelating agents and also improvement in renal manifestations (reduced proteinuria and increased e-GFR).

Conclusions: Our case’s uniqueness is the occurrence many years later the beginning of the therapy with zinc acetate dihydrate. This contrasts with previous theory since renal involvement with IgA nephropathy occurred despite the adequate pharmacological control of the copper dysregulation. This makes necessary steroid treatment in these patients. In conclusion, we suggest adding a screening for renal damage (creatinine and urinalysis) in the follow-up of patients with MW although under treatment and liver disease in remission.

No conflict of interest

POS-426

WHIPPLE DISEASE IN A PATIENT WITH MEMBRANOUS GLOMERULONEPHRITIS: FIRST CASE IN LITERATURE

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Introduction: The Whipple Disease (WD) is an extremely rare infective condition with an incidence of one individual in a million people, mainly attributed to the Tropheryma Whipplei (TW). It is described as a gram-positive belonging to the family of Actinomyces. Along with other factors, the genetic plays its role through the immunological hyperactivity towards TW. Here we report an atypical presentation of this disease, in a patient admitted to our Department several times.

Methods: Male patient, 46 years old, affected by essential epilepsy, treated with Carbamazepine, and a serum-negative rheumatoid arthritis treated with NSAID. The patient reported a right-sided hearing loss due to suspected viral infection and had a history of papillary thyroid carcinoma, treated with a total thyroidectomy and radiometabolic therapy. The patient was hospitalized to our Nephrology Unit for the onset of a nephrotic syndrome (24h-proteinuria 13640 mg/day) and US-guided renal biopsy was performed, where leading to a histological diagnosis of Membranous Nephropathy (MN) with high titre of serum PLA2R antibodies and normal kidney function (Tab.1). Because of his personal history of neoplasia, we could not follow KDIGO guidelines recommendations for MN, which indicate a first-line treatment with an alkylating agent alternated with cortisone for six months. Therefore we opted for a treatment with mycophenolate of 2g/die. Due to the failed remission, we started a treatment with Rituximab. The patient has been hospitalized three more times for the onset of dyspepsia, anaemia, joint pain, weight loss, diarrhea and fever, which have been studied by the following examinations (Tab. 2). In particular, a diffuse