Aims Vein of Galen arterial malformation (VGAM) is a rare high flow cerebral arteriovenous malformation which most commonly presents with cardiac failure in infancy. VGAM is considered to be a sporadic disorder, with a population incidence of 1 in 100,000. No genetic basis or increased risk of recurrence within affected families has been identified previously. Recently, RASA1 gene mutations have been identified as causative in the autosomal dominant capillary malformation arteriovenous (AV) malformation (CM-AVM) syndrome, a condition presenting with multiple skin AV malformations. A large European study of affected kindreds identified associated non-cutaneous AV malformations and, amongst 140 individuals, identified two cases of VGAM, raising the possibility of a genetic basis for this condition¹. The aim of the present study was to assess the frequency and type of RASA1 mutations in a population presenting with VGAM malformation.

Methods A National Centre for VGAM treatment obtained consent for RASA1 mutation analysis for all cases presented to the service from January 2011. Genomic DNA was obtained from blood samples and the 25 exons of the RASA1 gene were sequenced for each patient.

Results RASA1 analysis has been undertaken for 11 cases and four were positive for mutations: c.2912T > C (missense), c.2125C > T (truncated) and C.2119C > T (missense) (two cases). The two cases with the C.2119C > T mutation were siblings. One case, with the c.2125C > T mutation, developed the typical CM-AVM rash.

Conclusions RASA1 mutations are strongly associated with VGAM and are biologically plausible causative mutations. The autosomal dominant inheritance of this mutation, has a significant implication for counselling affected families.

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G26 LYMPHATIC DISORDERS IN NOONAN SYNDROME

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Aims To investigate the lymphatic phenotype in Noonan syndrome with reference to the medical literature

Methods Notes from patients with Noonan syndrome attending a lymphoedema clinic were located via the Geneworks database by searching for "Noonan syndrome" and then examining paper notes of those patients who had lymphoedema listed as a feature. The patients' letters and results stored in the Electronic Patient Register were also accessed and information on lymphatic abnormalities and molecular results was gathered and analysed. Images and results of lymphoscintigraphy were obtained from iSite Enterprise.

Results 7/582 Noonan syndrome patients (1.2%) had lymphoedema listed as a characteristic, and were included in this study.

The current age of patients ranged from 6 to 37 years. Onset of lymphoedema ranged from birth to 27 years, with a mean of 10.3 years.

5/7 patients had swelling of the lower limbs and genitalia. 5/7 had systemic involvement (intestinal lymphangiectasia, chylous reflux or chylothorax). 4/7 had genital lymphorrhoea.

Conclusion This study suggests that severe lymphoedema is a less common feature of Noonan syndrome than previous reports have indicated. Mild lymphoedema in the remaining patients, however, cannot be excluded. Within the patient group studied, a consistent pattern of lymphatic abnormality was seen: lower limb lymphoedema with variable age of onset, and genital involvement with chylous reflux.

G27

THE LYMPHATIC PHENOTYPE IN TURNER SYNDROME: AN EVALUATION OF PATIENTS PRESENTING TO THREE SPECIALIST PRIMARY LYMPHOEDEMA CLINICS AND LITERATURE REVIEW

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Aims This study aimed to analyse the medical records of a cohort of 19 Turner Syndrome patients attending three specialist primary lymphoedema clinics to elucidate the key features of the lymphatic phenotype of Turner Syndrome and provide vital insights into its diagnosis, progression and management. Lymphoedema of the hands, feet and cervical region is a common and key diagnostic indicator of Turner Syndrome, present in >60% of patients, though is poorly described in the literature.

Methods The study sample of 19 female patients was obtained from specialist primary lymphoedema clinics at three major centres and located by identifying all patients with Turner Syndrome and lymphoedema from hospital databases. Patient and genetic notes were identified through the use of patient-specific numerical identifiers. These notes were thoroughly analysed and examined and any important information inserted into a spreadsheet pro forma.

Results The majority of patients presented at birth with 4-limb lymphoedema which often resolved in early childhood but frequently recurred in later childhood. There was 1 case of systemic involvement (e.g. intestinal or pulmonary lymphangiectasia). The swelling was confined to the legs and hands with no facial or genital swelling. The most significant discovery from this research was a pattern observed from the lymphoscintigraphy results, which suggested that the lymphatic phenotype of Turner Syndrome may be due to lymphatic functional hypoplasia of lymphatic tracts.

Conclusion Turner Syndrome frequently presents at birth with 4-limb lymphoedema which often resolves in early childhood but may recur at any age. The lymphoscintigraphy results suggested that the lymphatic phenotype in Turner Syndrome may be due to lymphatic functional hypoplasia, a new perspective which may highlight the importance of this test as a baseline assessment of lymphoedema in Turner Syndrome patients.

G28

A NOVEL MISSENSE MUTATION IN KERATIN 1 UNDERLYING CLINICALLY MILD EPIDERMOLYTIC ICHTHYOSIS MIMICKING EPIDERMOLYSIS BULLOSA SIMPLEX SUPERFICIALIS

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Inherited skin peeling may be autosomal recessive (AR) or autosomal dominant (AD). When AR, this can be localised, as in acral peeling skin syndrome (APSS); or generalised, as in peeling skin syndrome (PSS) types A (non-inflammatory) and B (inflammatory). When AD, this can present in association with ichthyosis as either epidermolytic ichthyosis (EI) or superficial epidermolytic ichthyosis