SPUR TB TOO? WHAT IS ON THE MENU?

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BACKGROUND/AIM

Severe infections in the absence of secondary immunodeficiency can alert to single gene in-born errors of immunity, underlying susceptibility to specific infections. Mendelian Susceptibility to Mycobacterial Disease (MSMD) is a primary immunodeficiency (PID) characterised by errors of the IL12-IFN-y pathway. MSMD is defined by selective susceptibility to weakly virulent mycobacteria, Bacillus Calmette-Guerin (BCG) and other environmental mycobacteria in otherwise healthy individuals without overt immunological abnormalities. Presentation may include mycobacterium tuberculosis complex (MTBC), other invasive intra-macrophagic infections such as salmonella or mucocutaneous infections caused by candida species. These patients are often missed under the justification of an environment of hyperendemic TB exposure and poor treatment compliance but also due to lack of laboratory and clinical awareness. Severe, persistent, unusual or recurrent (SPUR) infections have been applied as clinical warning signs for PID and are proposed in the context of MSMD.

METHODOLOGY

Between 2013-2018 paediatric patients up to 15 years with SPUR TB infections were recruited through the Immunology Unit at Tygerberg Hospital (TBH). Severe TB was defined as poor host control of infection or complicated disease manifestation including disseminated TB (TB meningitis and miliary disease, persistent as infection not responding to treatment despite appropriate regimen and compliance, unusual site or infection and recurrent TB as more than one episode. Basic immunological screening then, focused immuno-phenotyping and whole exome sequencing (WES) was performed on each of the cases.

RESULTS

A total of 22 patients (4.4 per year) without secondary immunodeficiency were entered on the South African PID registry with a diagnosis of MSMD. Presentation with mycobacterium tuberculosis complex (MTBC) predominated (73%), poorly pathogenic mycobacteria were identified in 27% (6) of patients, 14% (3) with non-tuberculous mycobacteria (NTM) and 14% (3) with disseminated bacillus calmette-guerin (BCG). All presented with severe TB. Unusual infection (BCG or NTM) had a pathogenic variant in all cases. Functional work on the IFN-y IL-12 pathway was done on 45% (10/22) and all showed abnormal function with a varied phenotype. 40% of SPUR TB infections were identified with a known MSMD variant and 60% with a true variant requiring further functional validation. Treatment regimen was documented in 54% of cases and all required a longer duration of treatment than normal for disease.

CONCLUSION

In the paediatric population SPUR TB infections in the absence of secondary immunodeficiency should alert to further screening for PID. More than one episode of TB can signify MSMD as should poorly pathogenic TB in the absence of risk factors. Baseline immunological screening is usually normal, thus disease could be missed without focused immuno-phenotyping and molecular diagnosis. These patients often require longer duration or expert initiated individualised treatment to clear disease. The phenotypic presentation is wide in this hyperendemic region and regular MTBC infection with abnormal presentation should alert further investigation.

A NOVEL METHOD FOR MEASURING LYMPHOCYTE PROLIFERATION TO NON-SPECIFIC AND SPECIFIC STIMULANTS, USING KI-67 AND FLOW

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BACKGROUND/AIM

Primary immunodeficiencies (PIDs) are a group of hereditary conditions that also include various types of severe combined immunodeficiency (SCID) and combined immunodeficiencies (CIDs) affecting cellular and humoral immunity. T-cell proliferation tests are essential in the diagnostic work-up of these disorders. The current gold standard for measuring T-cell proliferation uses tritiated thymidine (3H) quantification – a radioactive marker for proliferation. This test requires large sample volumes, often collected from SCID patients who are generally small and underweight. In vitro T-cell function testing is carried out by inducing T-cell proliferation to various specific and non-specific stimulants. Indications for testing include suspected T-cell immunodeficiency and monitoring of T-cell response after haematopoietic stem-cell transplant.

The aim was to develop a T-cell-proliferation assay to mitogens and recall antigens based on the principle of flow-cytometric quantification of intracellular KI-67 and then comparing this method to the current gold standard. Benefits include the requirement of a smaller sample volume, increased cost-effectiveness for all parties, increased specificity and sensitivity, the elimination of the use of radioactive isotypes and increased efficiency.

METHODOLOGY

In the method, peripheral blood mononuclear cells (PBMCs) were stimulated by mitogens (Phytohemagglutinin, Pokeweed mitogen and Concanavalin A), phorbol 12-myristate 13-acetate (PMA), anti-CD3, Ionomycin, IL-2 and recall antigens (*Candida albicans*, varicella zoster and tetanus toxoid) respectively. Cells were allowed to proliferate for 3–6 days in complete media; depending on the stimulant used, after which they were labelled with surface and intracellular markers (KI-67) and subsequently analysed using flow cytometry.

RESULTS

Comparisons were made between the radioactive and the flow-cytometric methods, and 100% correlation as well as the reproducibility of results between the two methods were obtained.

CONCLUSION

We concluded that the flow-cytometric method is a suitable replacement for the radioactive method and that it will aid in the diagnosis of various T-cell immunodeficiencies.

ENVIRONMENTAL FACTORS ASSOCIATED WITH ALLERGY IN URBAN AND RURAL CHILDREN FROM THE SOUTH AFRICAN FOOD ALLERGY (SAFFA) COHORT

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BACKGROUND/AIM

The recently published South African Food Allergy (SAFFA) study indicates a clear rural and urban difference in allergy prevalence within a single country. Various protective and promoting environmental factors have been postulated to influence food and other forms of allergy. Dietary factors, including the consumption of unpasteurised cow's milk, fermented milk and the variety of foods introduced during infancy, were investigated. The influence of fast food, fried food and microwaved meat and vegetable consumption on allergy were also assessed. This study also investigated the role of a Westernised diet, high in advanced glycation end-products (AGEs), in allergy prevalence.

METHODOLOGY

Three hundred and ninety-eight rural and 1 185 urban children (12 months to 36 months of age) were screened for self-reported allergic symptoms, food sensitisation and challenge-proven food allergy. In addition, a sub-group of children (535 urban and 347 rural) was screened for aeroallergen sensitisation. Parents and/or guardians completed questionnaires on antenatal and post-natal environmental and food exposure, including unpasteurised milk and fermented milk products ('amasi'). A total of 535 urban and 398 rural participants completed questionnaires on fast-food consumption.

RESULTS

Overall, higher rates of allergic diseases were reported in rural as opposed to urban children. In the urban cohort, consumption

of 'amasi' was associated with lower rates of allergic rhinitis (AR) (16.8% vs 31.3%; p = 0.001), atopic dermatitis (AD) (21.3% vs 28.6%; p = 0.01) and self-reported asthma (5.3% vs 11.5%; p = 0.003). When compared to rural children, the consumption of food containing high advanced-glycation end-products (AGEs) was associated with significantly higher aeroallergen sensitisation rates in urban children (13.8% vs 2.8%; p = 0.01, OR 5.5; 1.6–19.1; p = 0.01). In rural children, a high consumption of fried and/or microwaved meat was associated with food sensitisation at 1 mm and 3 mm with odds ratios of 4.4 (CI 1.5–13.0; p = 0.01) and 5.0 (CI 1.2–19.9; p = 0.02) respectively. Furthermore, high consumption of fruit and vegetables by rural children was associated with significantly higher rates of self-reported asthma (5.7% vs 3.6%; p = 0.001), food sensitisation at ≥3 mm (8.9% vs 2.0%; p = 0.01) and food allergy (4.4% vs 0.0%; p = 0.001).

CONCLUSION

Early in life, rural exposure protects against some allergies in childhood. Urbanisation may hamper exposure to these modifiable, protective elements.

FLOW-CYTOMETRIC MEASUREMENT OF PROLIFERATING, KI-67 INCORPORATED LYMPHOCYTES FOR THE DETECTION OF METAL HYPERSENSITIVITY

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BACKGROUND/AIM

The incidence of metal sensitivity is increasing and is driven by the activation and proliferation of allergen-specific memory T-lymphocytes. Owing to its good sensitivity and reproducibility, a lymphocyte proliferation test (LPT) using tritiated thymidine incorporation is considered as the gold standard for detecting metal sensitivity in patients with clinical symptoms of a type-IV hypersensitivity to metal. Chronic low levels of exposure to metals in pacemakers, dental fillings and implants, joint prostheses, jewellery and environmental pollutants can lead to contact dermatitis and other localised allergy symptoms. The aim of this study is to compare the tritiated thymidine LPT with an in-house multi-colour flow-cytometric LPT method.

METHODOLOGY

Fifty samples were received for a tritiated thymidine LPT to test metal allergies and were run in parallel with the new Ki-67 flow-cytometric assay. Lymphocytes were cultured in microtitre wells with metal allergens for six days. Unstimulated cells, cells stimulated with metal allergens and a positive control were analysed to produce patient results. Stimulation indexes (SI) were calculated. SI <2 is considered as negative, SI between 2 and 3 is indeterminate and SI ≥3 is considered positive.

RESULTS

A high correlation between flow-cytometric LPT and tritiated thymidine LPT was observed: 38% tested negative and 36% positive on both methods. There was a discrepancy in 6% of the cases tested. Some 12% of the patients were border positive on the tritiated thymidine LPT method and positive on the flow-cytometric LPT method and 6% were border positive on the flow method but positive on the tritiated thymidine LPT method.

CONCLUSION

A good analytical performance and a high correlation were observed between the two methods. The optimised flow-cytometric LPT performs as well as the tritiated thymidine LPT in the identification of metal sensitisation. This methodology is a non-radioactive assay, requires less sample volume and is a good alternative to radioactive lymphocyte proliferation tests, which makes it more suitable for routine laboratory use.

PERINATAL EXPOSURES AND THEIR ASSOCIATION WITH ATOPIC DISEASES IN URBAN AND RURAL CHILDREN FROM THE SOUTH AFRICAN FOOD ALLERGY (SAFFA) COHORT

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BACKGROUND/AIM

The South African Food Allergy (SAFFA) study examines the prevalence of atopic disease and its influences in South Africa. Results show a difference in perinatal exposures between urban and rural children and the influences they have on the occurrence of atopic diseases.

METHODOLOGY

A total of 390 rural and 1 185 urban children (12 to 36 months of age) were screened for food allergy and food sensitisation. In addition, a sub-group of children (535 urban and 347 rural) was screened for aeroallergen sensitisation. Parents completed questionnaires on self-reported allergic symptoms, and on antenatal and post-natal exposure to farm animals, tobacco smoke and other indoor pollutants. Food allergy was identified by skin-prick testing (SPT) and oral-food challenges. Aeroallergen sensitisation was identified by SPT.

RESULTS

The rural children whose mothers smoked during pregnancy had higher rates of self-reported asthma (11.1% vs 0.8%; p = 0.002). The urban children whose mothers or fathers smoked had significantly higher rates of self-reported asthma than those who did not (13.1% vs 7.7%; p = 0.01 and 11.6% vs 7.0%; p = 0.001). Maternal smoking was associated with higher rates of allergic rhinitis (AR) and allergy in the urban cohort (32.1% vs 23.2%; p = 0.003, 50.4% vs 43.4%; p = 0.04). Among the urban children, 2.5% had weekly contact with farm animals compared to 99.3% of rural children (p = 0.001). The rural participants with no farm animal contact had significantly higher rates of aeroallergen sensitisation (50.0% vs 3.5%; p = 0.003), food sensitisation (33.3% vs 5.1%; p = 0.03) and food allergy (33.3% vs 0.3%; p = 0.001). The Caesarean section (CS) rate in the urban cohort was 40.5%, double that of the rural cohort of 18.8%. (p = 0.001). The urban children born via CS had double the food allergy rates of those born vaginally (3.3% vs 1.6%; p = 0.05).

CONCLUSION

Risk and protective factors differed between the urban and the rural settings. The urban black African participants resembled the rest of the urban cohort rather than the black African rural cohort. The loss of rural protective factors, particularly farm animal exposure, may expose an allergy risk which could have been kept in check. These factors are modifiable. Discouraging unnecessary CSs as well as increasing exposure to outdoor play are interventions that are feasible, and need to be addressed to avoid an increase in allergies in African countries running in parallel to the process of urbanisation.

ACQUISITION OF TOLERANCE TO EGG AND PEANUT IN BLACK AFRICAN FOOD-ALLERGIC CHILDREN WITH ATOPIC DERMATITS

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BACKGROUND/AIM

There are no previous data on tolerance development in children with atopic dermatitis (AD) and concomitant food allergy in low- and middle-income settings. The aim of this study was to determine the rate of tolerance acquisition to egg and peanut five years after diagnosing food allergies in South African children with AD, and to explore the factors influencing tolerance acquisition.

METHOLOGY

Five years after first diagnosing food allergy in 37 South African children with egg and/or peanut allergy, they were reassessed for their allergies by questionnaire, skin-prick tests (SPTs), ImmunoCAP-specific IgE (sIgE) tests (Thermo Fisher Scientific/Phadia, Sweden) to egg white, ovomucoid, peanut and Arachis hypogaea allergen 2 (Ara h 2) and by incremental food challenges.

RESULTS

Eighteen of 25 originally egg-allergic patients and 19 of 24 originally peanut-allergic children were followed up at median ages of eight years and three months and nine years and six months respectively. A high percentage of the children (72.2%) outgrew their egg allergy and 15.8% outgrew their peanut allergy. Allergic comorbidity remained high, with asthma increasing over time, and AD remaining moderately severe in the cohort overall. On diagnosis, sIgE egg white ≤9.0 kU/L and sIgE ovomucoid ≤2.0 kU/L were associated with tolerance development to egg five years later. At follow-up, sIgE egg white ≤0.70 kU/L, sIgE ovomucoid ≤0.16 kU/L, SPT egg-white extract ≤1 mm and SPT fresh egg ≤5 mm were associated with tolerance. At diagnosis, sIgE Ara h 2 ≤1.7 kU/L and SPT peanut ≤10 mm were associated with tolerance development to peanut five years later. At follow-up, sIgE peanut ≤0.22 kU/L, sIgE Ara h 2 ≤0.18 kU/L and SPT peanut ≤5.5 mm were associated with tolerance.

CONCLUSION

Egg allergy was outgrown in 72.2% and peanut allergy in 15.8% of a cohort of South African children five years after diagnosis of AD. This is in keeping with findings derived from studies in higher socioeconomic settings, and it can help to guide the counselling of patients with allergies to these foods of high nutritional value.

COMPARISON OF 23-VALENT PNEUMOCOCCAL IGG ELISA WITH 13-VALENT MULTIPLEX SEROTYPE-SPECIFIC PNEUMOCOCCAL ANTIBODY ASSAY AS A DIAGNOSTIC TOOL IN EVALUATING HUMORAL IMMUNE DYSFUNCTION

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BACKGROUND/AIM

Vaccine responses are used as a tool to test the functionality of the humoral immune system. The response to polysaccharide antigens in pneumococcal vaccines is currently determined by assessing IgG for 23-valent serotypes by ELISA. Serotype-specific pneumococcal antibody (SSPAb) is used for the diagnosis and therapeutic interventions of various primary immunodeficiencies (PIDs) as well as of functional secondary immunodeficiencies (SIDs).

The aim of this study is to compare the method agreement between the Binding Site 23-valent pneumococcal IgG ELISA (23vELISA) and an in-house 13-valent serotype-specific multiplex assay in evaluating vaccination responses in patients with suspected functional immunodeficiencies.

METHODOLOGY

As part of the routine diagnostic work-up for humoral immunodeficiencies, pneumococcal IgG ELISA is requested by clinicians. Patients are subsequently vaccinated with the polysaccharide vaccine (Pneumovax®23) and follow-up pneumococcal IgG levels are determined. Pneumococcal IgG levels at baseline and four weeks post-vaccination are measured using both assays.

RESULTS

Large variability in pre- and post-vaccination results for individual serotypes are observed. The main limitation of the 23vELISA assay is its inability to distinguish between high responses to a few individual serotypes and a good overall response. There is a good method agreement between 23vELISA and 13-valent multiplex for serotype-specific individual IgG thresholds.

CONCLUSION

Each patient should be assessed individually and their results interpreted with critical clinical judgement. In children vaccinated with conjugate pneumococcal vaccine (Prevnar®13), the World health Organisation (WHO) recommends a cut-off of ≥0.35 µg/mL for ≥50% serotypes as a 'protective' serotype IgG concentration. In adults, the American Academy of Allergy, Asthma & Immunology (AAAI) guidelines defined the 'protective' response to each pneumococcal serotype as an antibody level of ≥1.3 µg/mL for ≥70% serotypes. The multiplex SSPAb assay is robust and produces reliable results. This methodology requires less sample volume and less time than 13 individual ELISAs for SSPAbs and provides a more accurate determination of vaccine responsiveness as opposed to total pneumococcal IgG levels.

SEX HORMONE HYPERSENSITIVITY AND CHRONIC URTICARIA

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BACKGROUND/AIM

Although rare, urticarial exacerbations and cyclic hormone fluctuations of oestrogen and progesterone have been described in the literature. However, limited data regarding the incidence and prevalence of this association are found. In patients with chronic urticaria, sex hormones may trigger urticarial episodes, and such episodes have been associated with recurrent miscarriage. Owing to a lack of validated laboratory tests, a detailed history in relation to the menstrual cycle is key to a diagnosis of both progesterone and oestrogen hypersensitivity.

METHODOLOGY

CASE REPORT

Patient AH, a 32-year-old woman, P3G3, has had a chronic history of urticaria for the past five years. The onset was soon after the birth of her first child. The urticaria has become increasingly worse, with associated angioedema. It flares up monthly several days prior to menstruation. During pregnancies, the urticaria improves and flares up as she starts to wean breastfeeding. Prior to our consultation, AH had tried various elimination diets, including preservative-free diets, which had no effect on the urticaria. She does not take anti-inflammatory drugs. Clinically, she had urticarial lesions on her legs and abdomen, and the rest of the examination was normal.

RESULTS

FBC, CRP, ESR, TSH and thyroid antibodies, and urine dipstick, were normal. Skin prick testing (SPT) was deferred as she was eight weeks pregnant.

CONCLUSION

This patient has a possible diagnosis of progesterone hypersensitivity. This is based on the cyclic nature of the worsening of her urticarial reactions at peak progesterone levels during the luteal phase of her menstrual cycle. This is also supported by the improvement of her symptoms post-partum when lactating, as progesterone levels drop. Previous studies have suggested SPT using oestrogen and progesterone during the luteal phase, and assessing both immediate and delayed reactions. In summary, data on hormone sensitivity are very limited and improved diagnostic tests are needed.

THE USE OF FLOW-CAST TESTING FOR FOOD-ADDITIVE HYPERSENSITIVITY IN JOHANNESBURG

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BACKGROUND/AIM

Preservatives are often implicated in allergic disease such as chronic idiopathic urticaria, angioedema, asthma and anaphylaxis. This is contrary to the current literature, which reports that such reactions to food additives are in fact very rare, with proven cases being 0.23% in a large population-based study. The exception is sulphites, which have been shown to exacerbate asthma in a small group of asthmatic patients. An in vitro tool, the flow-cytometric basophil activation test (BAT), is used to assess basophil-activation marker expression following antigen stimulation. It is a very useful test because it can be used in allergic disease where the mechanism is unclear. This is because it detects both IgE-mediated responses and non-IgE-mediated hypersensitivity. This article examines the frequency with which FLOW-CASTS (basophil activation tests) are ordered by doctors at one of the main laboratories in Johannesburg, and how often these tests yield positive results.

METHODOLOGY

A purposive sampling method will be used to select expert information sources from Lancet laboratories.

RESULTS

The final results will be presented in the form of a table.

CONCLUSION

Although the majority of FLOW-CASTS yield negative results, those that are positive are most commonly for sodium benzoates and sodium salicylates.

PIT LATRINES AND LATRODECTISM: AN ADDITIONAL RISK FACTOR FOR SPIDER BITES IN RURAL SOUTH AFRICA

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BACKGROUND

The epidemiology of spider bites by the *Latrodectus* species was well studied in South Africa in the early 1990s and later reviewed in the early 2000s. Risk factors that were found to be directly linked to cases involving *Latrodectus* species included occupations such as construction workers, agricultural workers, municipal and utility workers, domestic workers and entomologists.

CASE REPORT

According to the South African nationwide census of 2011, it was discovered that 57% of the population of the country used flush toilets (16 million people), 31% pit toilets (16 million people), 3% chemical toilets (1.5 million people) and 2% bucket toilets (1 million people). The dark, moist, filthy and insect-predominant nature of pit toilets serves as an ideal habitat for spiders. We report three cases of *Latrodectus* spider bites that occurred while using a pit latrine in rural south-eastern South Africa, with one case of black widow penile spider bite resulting in a severe case of latrodectism requiring antivenom administration.

CONCLUSION

We propose that pit latrines should be considered as an additional risk factor for *Latrodectus* spider bites in rural South Africa. These should be reported to local authorities for strategies to ensure their much-needed elimination.

DRUG REACTION: MOBILE HEALTH APPLICATION FOR PERIOPERATIVE ANAPHYLAXIS

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BACKGROUND/AIM

In 2018, the Royal College of Anaesthetists published their sixth national audit (NAP6) – the most complete representation of perioperative anaphylaxis ever assembled. The report details the perioperative incidence, management, investigation, referral, specialist allergist management and incident reporting

that led to the more than 100 recommendations included in the report. The Drug Reaction smartphone application was developed with these recommendations in mind to address the void in perioperative hypersensitivity management and simplify communication. The ultimate goal is improved service quality and patient safety.

METHOLOGY

In the event of a suspected allergic reaction in the perioperative period, the anaesthetist logs relevant data through a quick referral page. Reminders will be sent to the relevant anaesthesiologist for the timely acquisition of three separate mast-cell tryptase blood samples. Drug Reaction uses location detection to refer the patient to the closest available allergy clinic. A letter is emailed to the patient describing the event, including possible culprits, with advice on how to access this information in the case of medical contact before the date of the allergy clinic visit. During the visit, the allergist has access to relevant incident information as entered on the application at the time of the event as well as the mast-cell tryptase results. The results of the allergist evaluation can be entered effortlessly into the application. Uploading this data leads to five automated processes:

1. These results will appear on the application when the patient's details are entered during any future interaction with doctors or pharmacists.
2. The patient receives a letter via email informing them of the results of the test.
3. The referring physician receives a letter via email informing them of the results of the test.
4. The results are reported to Health Products Regulatory Authority.
5. The patient's Health ID on their smartphone is auto-populated with the proven culprit/drug.

CONCLUSION

'Patients have a right to expect that their suspected perioperative drug reaction will be investigated promptly and expertly, so that they are aware of the drugs and other substances they can receive safely in the future, and those they should avoid.'

AUTOIMMUNITY IN HEREDITARY ANGIOEDEMA: A DIAGNOSTIC CHALLENGE

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BACKGROUND/AIM

Isolated angioedema, in the absence of urticaria and other allergic manifestations, suggests a C1 esterase inhibitor (C1 INH) deficiency, either the rare hereditary angioedema (HAE) or the much rarer acquired angioedema (AAE). In the work-up for C1 INH deficiency-associated angioedema, a full-complement system evaluation becomes necessary. A finding of hypocomplementaemia and autoantibodies against the components of the complement system adds hypocomplementaemic urticarial vasculitis syndrome (HUVS) as a differential diagnosis to HAE and AAE.

METHODOLOGY

A case report of a patient seen at an allergy clinic who presented with recurrent, isolated angioedema.

RESULTS

A 13-year-old RVD non-reactive boy was referred to our allergy clinic with a long-standing history of isolated angioedema affecting mostly the face, upper chest, penis and larynx. This has occurred since early infancy. A typical episode would last for 3–5 days following a course of systemic steroids and antihistamines. He would have more than three episodes a year without any obvious precipitants or triggers. There is no positive family history. There are also no clinical or biological signs of arthritis, lupus or a lymphoproliferative condition.

Specific allergy testing was negative with normal FX5 and Phadiotop. Thyroid function and biochemistry were also normal. He exhibited classical pathway-mediated complement consumption with undetectable levels on CH 100, low C4 (0.06) and low C1-INH (0.04) levels. However, he had normal C3 levels and had very high levels of circulating anti-C1 q levels (>100). On a further autoimmunity screening, he had a positive ANA with an absence of other autoantibodies.

CONCLUSION

Elevated anti-C1q antibodies are commonly found in patients with HUVS and AAE. However, a small percentage of patients with HAE (0.2–4%) have been reported to have these auto-antibodies. In view of the angioedema without urticarial vasculitis, presentation within the first year of life, the presence of normal C3 levels with C1 INH deficiency and a rapid response to fresh-frozen plasma, the patient was diagnosed with hereditary angioedema and was commenced on long-term prophylaxis. The presence of anti-C1q antibodies in a patient with C1 INH deficiency-related angioedema presents a diagnostic challenge and should include a work-up for HAE, HUVS and AAE.

COMPLICATIONS OF DELAYED DIAGNOSIS IN PRIMARY IMMUNE DEFICIENCIES

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BACKGROUND/AIM

Primary immune deficiencies (PIDs) are a heterogenous group of hereditary disorders of the immune system. As a group, PIDs are more common than previously thought. Early diagnosis of PID is essential to prevent associated morbidity and mortality. Simple screening tests are cheap and readily available. However, a delay in diagnosis is frequent due to a lack of awareness of these conditions.

METHODOLOGY

We report on a HIV-uninfected male patient who presented at the age of five months with an interstitial pneumonia unresponsive to therapy. PID work-up revealed hypogammaglobulinemia, but the mother refused further treatment. The boy presented again at four years of age with a two-month history of productive cough unresponsive to oral antibiotics. Clinically, he was well-grown, not clubbed and with a normal chest examination. He had peri-anal vitiligo. A CT chest revealed mild bronchiectasis. Markedly reduced serum levels of IgG with normal to high IgM levels were found. B- and T-cell counts were normal. Liver function tests were deranged. Cryptosporidium PCR, on the stool, was positive and an abdominal sonar demonstrated cirrhosis. Because of the severe hypogammaglobulinemia with normal IgM level, hyper-IgM syndrome (HIGM) was suspected.

RESULTS

Classed-switched memory B cells were low and the CD40 ligand was absent, confirming a diagnosis of HIGM. Immune globulin replacement therapy (IRT) and cotrimoxazole prophylaxis were commenced. No further respiratory-tract infections have occurred. Currently, the main concern is cryptosporidium infection with associated liver cirrhosis. No treatment is available in South Africa.

CONCLUSION

HIGM is a combined immune deficiency leading to an increased susceptibility to sinopulmonary and opportunistic infections. Patients suffer from significant morbidity (such as bronchiectasis and liver cirrhosis) and mortality (20% survival by age 25 years). A normal IgM concentration does not exclude this condition and the diagnosis should be considered in children presenting with severe infections in the presence of hypogammaglobulinemia associated with a normal or high IgM serum level. Early management with IRT and allogeneic hematopoietic stem-cell transplantation before the onset of severe liver disorders can cure the disease; therefore, early diagnosis is of utmost importance.

BASELINE CHARACTERISTICS OF A COHORT OF CHRONIC SPONTANEOUS URTICARIA PATIENTS IN CAPE TOWN, SOUTH AFRICA

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BACKGROUND

Chronic spontaneous urticaria (CSU) and angioedema is a morbid condition with recently improved biologic treatment options. No data on cohorts in sub-Saharan Africa are available. In September 2018, the first UCARE centre on the African continent was certified. We aimed to review the baseline clinical, laboratory and treatment characteristics of our CSU patients present at our UCARE centre in Cape Town, South Africa.

METHODS

A prospective cohort of CSU patients was referred to our UCARE centre between January 2018 and April 2019. Baseline doctor and patient questionnaires, (clinician-led) laboratory investigations and UQoL-forms were completed.

RESULTS

A total of 77 patients were seen in the clinic and 30 consented to have their data reported. CSU occurred across ethnicities, with 50% of patients self-reported as being of mixed ancestry and 14% African; 80% were female. The majority of patients experienced both urticaria and angioedema (70%), with only 20% and 10% having either urticaria or angioedema only. In 60% of cases, urticaria affected the whole body, whereas angioedema predominantly affected the lips (66%), eyelids (46%) and the rest of the face (43%). A high frequency of gastric symptoms was observed (34%) and sleep disturbance was common (81%). Only 26% of patients were on high-dose antihistamine at their initial UCARE consultation, whereas 16% were on chronic corticosteroids. Despite motivations, only 7% of patients were able to access omalizumab.

CONCLUSION

The baseline clinical characteristics of our CSU patients are similar to those of other settings. CSU occurred across ethnic groups. Guideline-driven treatment outside of our UCARE centre was poor. The use of omalizumab was very limited, largely due to cost constraints.