UWOMJ

SUMMER SUPPLEMENT
VOLUME 80, ISSUE S1
The importance of learning outside the classroom and teaching others

As I sat down to read this year's case report submissions to our summer supplement I came to the realization that my decision to not participate in a summer clinical elective was a mistake. I deprived myself of a valuable learning experience. My fellow students, who seized hold of this opportunity, gained precious knowledge that cannot be learned by sitting in a classroom. Reading about their experiences made me realize that the famous physician Sir William Osler was wise when he stated, "Medicine is learned by the bedside and not in the classroom. Let not your conceptions of disease come from words heard in the lecture room or read from the book. See, and then reason and compare and control. But see first".

I invite you to read our fellow students’ case reports and learn vicariously through their writing as they teach us the knowledge they gained this summer at the bedside and not in the classroom. As you read these pages Sarah O'Connor will teach us an approach to narrow a differential diagnosis of hypotonia in a pediatric population. Jeff Landreville will describe the management of diabetic foot syndrome: a condition we will all likely encounter during our medical training. Lilian Wong will teach us why it is important to be an astute clinician, as she describes the presentation of Graves’ disease in an elderly patient. You will also learn about a rare tumour of the GI tract as Mark Xu tells the tale of a gastric schwannoma. The importance of multidisciplinary management is evident as Arielle Mendel teaches us about the complications of scleroderma. Lauren Sham reminds us that multiple sclerosis can also affect children and outlines the treatment options available to the pediatric population. Lastly, Abdul Naeem brings to our attention a complication of topical corticosteroid use that will be useful knowledge when we prescribe it for our future patients.

The writing of a case report is a time consuming process; yet, it is an important method to disseminate medical knowledge gained through clinical experiences. Our fellow students are to be commended for undertaking the challenge and contributing to our learning beyond the classroom. It is also important that we recognize the exceptional mentorship role undertaken by their supervising clinicians. These clinicians not only undertook the responsibility of supervising a junior medical student but also provided a valuable learning experience and the opportunity for scholarly growth. They are also to be commended for their efforts. We should all aspire to this standard and engage in opportunities to teach others during our future medical careers.

I hope that you enjoy this year's summer supplement and embrace future opportunities to learn outside the classroom and teach others.

Melissa J. MacPherson, PhD
Junior Associate Editor
CASE

Mrs. RS, a previously healthy 60-year-old lady, was referred to the Endocrinology clinic by her family physician for assessment of low TSH and elevated free T4. Over the last 2 months, she had been experiencing a sensation of neck tightness, mild dysphagia, hoarse voice, dry nose and some blood in her sputum every week. She also complained of frequent epistaxis ranging from blood in mucous to frank red blood from her nose with dizziness. Her appetite was increased and she believed that her body “doesn’t absorb anything well”. She had no weight loss. Mrs. RS does not have cold or heat intolerance. Her other complaints included fatigue, feeling anxious and irritable, and blurry vision when reading at nighttime with the occasional white flash. Her last optometry visit was 7 years ago.

She admitted to having seasonal allergies that have been improving over the last 10 years, for which she took over-the-counter allergy medications in the past. She has also used Nasonex for her nose in the past, prescribed by her family doctor. Her current medications include vitamins, Fosamax, calcium, magnesium and glucosamine. She denied taking any herbal supplements. She has no known drug allergies.

Her past medical history is significant for thyroid disease 10 years ago. She was unsure of the type of disease, but recalls taking medications for 2 years and stopping when her disease subsided. She also had a history of osteoarthritis (OA) in her hands for 8 years.

Her family history is significant only for OA in her mother. She denied any family history of thyroid disease. Mrs. RS has also had no surgeries or hospitalizations.

Her social history revealed that Mrs. RS is originally from the Philippines, of Chinese descent, and immigrated to Canada 20 years ago. She lives with her husband, her son, her daughter-in-law and her 2 grandsons. She works part-time in a coffee shop. She has never smoked cigarettes or used recreational drugs, and only has one drink at Christmas.

On examination, Mrs. RS sat comfortably in no apparent distress. Her weight was 100 lbs with a height of 5 feet 5 inches. Heart rate was 72 beats/minute and regular with a blood pressure of 110/60 mmHg and a respiration rate of 16 breaths/minute. Upon head and neck exam, she had full ocular movements with no lid lag, retraction or proptosis. Her thyroid was normal to palpation, with no lumps or enlargement. There was a soft painless lymph node in her right posterior cervical chain that measured under 1 cm. Auscultation of her thyroid revealed no bruits. Nasal conchae looked red and dry with dried blood.

Her lab results from her referral showed a TSH <0.05 mIU/L, free T4 25 pmol/L. Neutrophils were reduced at 1.7x10^9/L. B12 was decreased at 160 pmol/L.

Mrs. RS was diagnosed with recurrent Graves’ disease and started on methimazole 5 mg daily. Her TSH, free T3 and free T4 will be followed regularly. She was advised to return to her family doctor for B12 injections and follow-up for her epistaxis, most likely due to allergic rhinitis. Additionally, she was counseled to consult optometry for her vision changes.

DISCUSSION

Graves’ disease is increasing in prevalence, affecting about 1% of Canadians, and more common in women than men. Thyroid stimulating IgG antibodies (TSI) circulate in the body and activate the thyrotropin receptor resulting in follicular hyperplasia and hypertrophy. This enlarges the thyroid and increases thyroid hormone (T3 and T4) production. Excess T3 and T4 work on the pituitary, the heart, the liver, bone, reproductive organs, fat and muscle resulting in manifestations of thyrotoxicosis, summarized in Table 1.

Diagnosis of Graves’ disease can be made clinically by evaluating patients for hyperthyroidism signs and symptoms. Symptoms include weight loss, heat intolerance, insomnia, tremor, increased defecation, proximal muscle weakness, irritability, menstrual irregularity and erectile dysfunction with decreased libido and possible gynaecomastia in men. Signs include tachycardia, “Graves’ stare”, lid lag, proptosis, goiter, resting tremor, hyperreflexia, warm and moist skin. Rarely, patients can present with pretibial myxedema and thyroid-induced clubbing. Usually, patients will report increased appetite and food intake with paradoxical weight loss.

The case patient, Mrs. RS, did not present to clinic with overt hyperthyroidism symptoms and only reported similar anxiety and irritability that she experienced during her past thyroid problems. Notably, the irritability was “out of her control” and was starting to impact her home and work environments. Otherwise, her history and physical were within normal parameters. This “apathetic hyperthyroidism” is more typical in older patients who present with weight loss or depression. Compared to younger patients, they are less likely to exhibit tachycardia, tremor, goiter, exophthalmos or increased appetite.
Table 1: Thyroid hormone action and resulting manifestations of thyrotoxicosis

<table>
<thead>
<tr>
<th>System</th>
<th>Action of thyroid hormones</th>
<th>Manifestations of thyrotoxicosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pituitary</td>
<td>Suppress TSH production</td>
<td>Decreased TSH in labs</td>
</tr>
<tr>
<td>Cardiac</td>
<td>Increased channel expression, increased α-MHC and decreased β-MHC expression, increased serum atrial natriuretic peptide</td>
<td>Increased heart rate and contractility</td>
</tr>
<tr>
<td>Hepatic</td>
<td>Increased D1 deiodinase, LDL and VLDL receptors, lipase, and liver metabolism enzymes</td>
<td>Increased peripheral T₃ production, reduced total cholesterol, LDL cholesterol and lipoprotein(a)</td>
</tr>
<tr>
<td>Skeletal</td>
<td>Increased osteocalcin, alkaline phosphatase</td>
<td>Increased bone turnover, osteopenia, osteoporosis and fractures</td>
</tr>
</tbody>
</table>
| Reproductive | Male: increased sex hormone globulin and reduced free testosterone  
|            | Female: antagonism of estrogen action, impaired gonadotropin regulation                      | Male: erectile dysfunction, decreased libido  
|            |                                                                                              | Female: irregular menses                                                                        |
| Metabolic | Increased fatty acid oxidation and sodium-potassium ATPase                                  | Increased thermogenesis and oxygen consumption                                                     |
| White fat | Increased adrenergic lipolysis                                                               | Reduced fat mass                                                                                  |
| Muscle    | Increased SERCA activity, and serum creatinine kinase                                        | Proximal muscle weakness, fatigue                                                                |


Investigations to confirm Graves’ disease include suppressed serum TSH and elevated T₃ and T₄ levels. T₃ levels in Graves’ are elevated greater than T₄ due to action of thyroid hormones on the liver producing more D1-iodinases for peripheral conversion of T₄ to T₃. Further testing for TSI antibodies and radioactive-uptake scans may be useful in some patients; however, they are not necessary for diagnosis or management of Graves’ disease. In Graves’ patients, TSI antibodies would be present in the blood and the thyroid would have elevated uptake of radioactive iodine homogeneously.² As such, with TSH <0.05 and free T₄ elevated, the case patient RS has Graves’ disease.

Treatment of Graves’ disease includes three options: antithyroid medications, radioactive iodine ablation and surgical management.⁴ Antithyroid medications include the thionamides, propylthiouracil (PTU) and methimazole (MMI), which inhibit thyroid peroxidase and subsequent thyroid hormone synthesis.⁴ MMI is more effective than PTU and with less adverse reactions even on higher doses.⁵ PTU is favoured during pregnancy as MMI is rarely associated with teratogenicity: aplasia cutis and gastrointestinal defects. Thionamides are generally started until patients are euthyroid, then withdrawn for remission of Graves’ disease. However, the estimated recurrence rate of Graves’ on thionamides is estimated to be 50-60%,⁶ as was in the case of Mrs. RS. Thionamide-induced hypothyroidism correlates to a higher remission rate.⁶ Radioiodine (I-131) ablation is used to induce hypothyroidism to prevent recurrences of Graves’ disease and is 80% effective. Least often, surgical thyroidectomy can be used but is reserved for patients with complications of antithyroid medication, those who decline radiiodine and those with large goiters or thyroid nodules.² Total thyroidectomy has similar complications as subtotal thyroidectomy, however ST has a 30% recurrence rate for Graves’⁷ and thus total thyroidectomy is preferred.⁸ Generally, in non-pregnant patients without hepatic disease, the initial treatment for Graves’ disease is MMI.

Recurrence of Graves’ disease is treated similar to naïve Graves’ disease. However, some patients may need definitive treatment with radioiodine or thyroidectomy. These patients are usually hypothyroid post-treatment and are treated with L-thyroxine until their TSH values are within normal parameters.

**CONCLUSIONS**

Graves’ disease is a common problem presenting to family physicians and endocrinology clinics. Despite the typical textbook presentations of Graves’ disease, individual patients’ signs and symptoms are varied and one needs to seek context with laboratory confirmation to make the diagnosis. Treatment is also individualized to patient needs and can include antithyroid medication, radioiodine (RAI) ablation or thyroidectomy. Recurrence rates are 50-60% with antithyroid drugs, 20% in RAI ablation, 30% in subtotal thyroidectomy and <1% in total thyroidectomy. Recurrences are treated similarly to naïve disease. Recognition and treatment of recurrences of Graves’ disease are important to reduce complications and increase patients’ quality of life.

Resources for patients with Graves’ disease: National Graves’ Disease Foundation (www.ngdf.org), the American Thyroid Association (www.thyroid.org/patients/patients.html) and the Thyroid Foundation of Canada (www.thyroid.ca).
REFERENCES


An approach to the “floppy child”: clinically narrowing the differential diagnosis of hypotonia in the pediatric population

Sarah O’Connor (Meds 2014)
Faculty Reviewer: Dr. R. Garth Smith MB, BS, FRCPC (Department of Pediatrics, Queen’s University)

INTRODUCTION
Hypotonia, defined as a reduced tension in a muscle at rest, is a relatively frequent presentation in both the infantile and childhood period. It must be differentiated from muscle weakness (a reduction in muscle power, that may or may not accompany hypotonia), and laxity (an increase in joint range of motion that often accompanies hypotonia).

The possible causes of hypotonia in an infant or child are numerous, and include problems with: the brain, the spinal cord, the peripheral nerves, the neuromuscular junction, and skeletal muscles. The clinical exam of the hypotonic infant or child will yield many clues that the astute physician (or medical student) may use to narrow this broad differential diagnosis and to focus subsequent investigations. This case report will allow the student to develop an approach to hypotonia in the pediatric population.

CASE
MS is a 2 year old boy who initially presented to his family physician at approximately 18 months when his parents noticed he was walking with his feet turned out, and that he displayed a “waddling gait”. At the time, the parents mentioned that their son had difficulty keeping up with other children when walking, and would frequently trip when running. MS was subsequently referred to a general pediatrician, who noted proximal muscle wasting in the lower extremities, and calf hypertrophy bilaterally. MS was also described as exhibiting a positive “Gower sign”. A referral was made to an orthopedic surgeon, and X-rays of the lower limbs revealed no bony abnormalities. Upon consultation with neurology, the patient was admitted to Kingston General Hospital (KGH), and several diagnostic investigations were performed. The results of these investigations lead to a definitive diagnosis and a referral was made to the Child Development Centre (CDC) in Kingston, ON for follow-up care. To encourage reader involvement in formulating a differential diagnosis for this case, MS’s diagnosis will not be revealed until the end of this article.

MS presented with his parents in consultation at the CDC at the age of 2 years and 1 month. Past medical history revealed a complicated pregnancy, with his mother having a serious kidney infection requiring hospitalization at 36 weeks. At birth, there was meconium staining of the amniotic fluid, and MS required suctioning and in-hospital observation for 4-5 days. He initially had trouble feeding (would gag for the first few days), but subsequently, his mom reported no history of gagging, choking, or trouble swallowing. Functionally, MS is currently able to eat with a fork and spoon, although his mother has noticed a tremor in his hand at times. He is progressing well with regards to language development, with a large vocabulary, and saying several two-to-three word sentences. Adaptively, he is able to feed himself, and is showing interest in being toilet-trained.

Physical examination revealed a pleasant, engaging young boy who was very cooperative with most aspects of the exam. He tended to preferentially sit in a “W-posture” for enhanced stability. His gait is waddling and shows a wide-based stance. He likes to climb, although he has difficulty, and will often pull on the edge of his shorts to lift his legs up and over obstacles. MS demonstrates a positive “Gower sign” when getting up from the ground. His tone is decreased and there is significant hypermobility of all joints. Deep tendon reflexes (DTRs) are absent in the lower limbs bilaterally. Proximal muscle weakness is present both in the upper limbs (difficulty throwing a ball over his head), and the lower limbs (will tug on his shorts when performing a seated leg raise to kick at a ball). MS has functional fine motor skills that allow him to participate in a variety of activities. He uses a mature pincer grasp for picking up small objects, and uses an age-appropriate grasp when holding a marker. MS does have a noticeable tremor when completing activities requiring fine precision.

DISCUSSION
This section of the article will aid the student in developing and narrowing the differential diagnosis for the presented case.

Distinguishing upper motor neuron disorders from lower motor neuron disorders
The upper motor neurons (UMN) originate in the motor cortex of the brain and carry motor information to the spinal cord. Pediatric disorders of the UMN (characterized by hypertonia, increased DTRs, presence of the Babinski reflex, and an absence of muscle atrophy) include certain types of cerebral palsy, and chromosomal abnormalities (Table 1).

The lower motor neuron (LMN) carries motor information from the brainstem or spinal cord out to the skeletal muscles. LMN disorders are characterized by hypotonia, muscle weakness and possible atrophy, and reduced or absent DTRs (Table 1).

Examining MS revealed a boy with hypotonia, muscle weakness, and absent DTRs, consistent with the presentation of a LMN disorder. Once the disorder has been identified to affect the LMN, the physician must further narrow the differential diagnosis by determining the portion of the LMN that is affected.

Distinguishing between different LMN disorders
The LMN is composed of the anterior horn cell of the spinal cord, the peripheral nerve, the neuromuscular junction, and the skeletal
Diagnosis

Investigations at KGH revealed a normal creatine kinase (CK) level, ruling out the possibility of Duchenne’s muscular dystrophy (DMD). Subsequent EMG studies revealed normal functioning of the lower limb motor units, suggesting a neurogenic cause of the hypotonia and weakness. Genetic testing was done and was positive for spinal muscle atrophy (SMA).

SMA is an inherited degenerative neuromuscular disorder with a birth incidence of approximately 1 in 10,000. It affects the anterior horn cells of the spinal cord and can be clinically separated into four classes based on age at onset and developmental milestones achieved (Table 3). Based on his presentation, it is likely that MS has Type IIIa SMA, although further monitoring is required to confirm this. There is no known effective treatment for SMA. Patients receive supportive care to manage symptoms and prevent complications such as scoliosis and joint contractures. The prognosis varies considerably depending on SMA type and age at onset. MS will be followed every six months by the neuromuscular team at the CDC.

Conclusion

This case illustrates the importance of a thorough history and physical exam in the diagnosis of neuromuscular disorders in the hypotonic infant or child. Through careful deduction, the prudent physician or student can arrive at a narrow differential diagnosis, eliminating the need for unnecessary diagnostic testing, which is of benefit to both young patients and their families.

Table 1: Clinical Distinction between Upper Motor Neuron and Lower Motor Neuron Lesions

<table>
<thead>
<tr>
<th>Clinical Sign</th>
<th>Upper Motor Neuron (Corticospinal Tract)</th>
<th>Lower Motor Neuron (Neuromuscular)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tone</td>
<td>Increased (spastic)</td>
<td>Decreased</td>
</tr>
<tr>
<td>Reflexes</td>
<td>Increased</td>
<td>Decreased</td>
</tr>
<tr>
<td>Babinski reflex</td>
<td>Present</td>
<td>Absent</td>
</tr>
<tr>
<td>Atrophy</td>
<td>Absent</td>
<td>Possible</td>
</tr>
<tr>
<td>Fasciculations</td>
<td>Absent</td>
<td>Possible</td>
</tr>
</tbody>
</table>


REFERENCES

Table 2: Peripheral nervous system disorders

<table>
<thead>
<tr>
<th>Location of Lesion</th>
<th>Typical Findings</th>
<th>Examples of Cause†</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Motor</td>
<td>Sensory</td>
</tr>
<tr>
<td>Anterior Horn Cell</td>
<td>Weakness and atrophy in a segmental or focal pattern; fasciculations</td>
<td>Sensation intact</td>
</tr>
<tr>
<td>Spinal Roots and Nerves</td>
<td>Weakness and atrophy in a root-innervated pattern; sometimes with fasciculations</td>
<td>Corresponding dermatomal sensory deficits</td>
</tr>
<tr>
<td>Peripheral Nerve—Mononeuropathy</td>
<td>Weakness and atrophy in a peripheral nerve distribution; sometimes with fasciculations</td>
<td>Sensory loss in the pattern of that nerve</td>
</tr>
<tr>
<td>Peripheral Nerve—Polyneuropathy</td>
<td>Weakness and atrophy more distal than proximal; sometimes with fasciculations</td>
<td>Sensory deficits, commonly in stocking-glove distribution</td>
</tr>
<tr>
<td>Neuromuscular Junction Muscle</td>
<td>Fatigability more than weakness</td>
<td>Sensation intact</td>
</tr>
<tr>
<td></td>
<td>Weakness usually more proximal than distal; fasciculations rare</td>
<td>Sensation intact</td>
</tr>
</tbody>
</table>

†Note: disease examples altered from original source to apply to pediatric population.


Table 3: Classification on infantile SMA

<table>
<thead>
<tr>
<th>SMA type</th>
<th>Definition</th>
<th>Prognosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>I (Werdnig-Hoffmann)</td>
<td>Onset &lt; 6 months, never sat</td>
<td>Death usually within the first years of life, chronic courses in about 10 %</td>
</tr>
<tr>
<td>II (intermediate)</td>
<td>18 months, sits and stands with support, unaided walking not achieved</td>
<td>Survival mostly into adulthood.</td>
</tr>
<tr>
<td>III (Kugelberg-Welander)</td>
<td>IIIa &lt; 3 years, walks with early difficulties IIIb 3 – 30 years, normal motor development</td>
<td>Lifespan generally not reduced, variable ambulatory period</td>
</tr>
</tbody>
</table>


UWOMJ I 80:S1 I Summer 2011
Approach to treatment decision making in an aggressive case of pediatric multiple sclerosis

Lauren Sham (Meds 2014)
Faculty Advisor: Dr. Brenda Banwell MD, FRCPC (Department of Pediatric Neurology, Hospital for Sick Children)

CASE
A 13 year old previously well female presented in April 2011 with nausea, vertigo, mild gait ataxia, diplopia and fatigue. Her initial MRI (Figure 1) showed more than 20 hyperintense lesions on T2 FLAIR that were >3 mm in size throughout the supratentorial white matter, with multiple lesions in periventricular and corpus callosal areas. Contrast enhancing lesions were found in the right frontal lobe subcortical white matter, projecting from the corpus callosum, in the optic chiasm and superior cerebellar peduncle. Multiple T1 hypointense black holes were also found. MRI features met McDonald 2010 criteria for multiple sclerosis (MS). Spinal fluid was positive for oligoclonal bands. She was treated with a 5 day course of IV solumedrol then prednisone at 50 mg/d at 10 day taper. The family was counseled for high risk of recurrent symptoms and diagnosis of MS. At the end of her course of IV steroids she had a near full neurological recovery with some mild residual sensory deficits.

In May 2011, she began to experience left sided numbness below her neck and down her leg and exhibited a positive L’Hermitte’s sign (a classic finding in MS: an electrical sensation running down the back, often elicited by bending the head forward). These new neurological symptoms localizing to the spinal cord were distinct from her initial presentation, which was more than 30 days previous to this attack. This allowed further confirmation of MS diagnosis using Poser clinical criteria. Steroid treatment was not initiated as the patient did not find these sensory symptoms bothersome. The MRI at this point showed some lesions decreased in size, and one new gadolinium enhancing lesion indicative of active inflammation. Follow up MRIs in July and August 2011 showed multiple new hyperintense lesions in the brain and spinal cord including the brainstem, some of which were gadolinium enhancing, and some older lesions increased in size.

DOES SHE HAVE MS?
There have been several iterations of the diagnostic criteria for MS. This patient meets Poser Criteria for MS: 1 two attacks and clinical evidence of two separate lesions involving different parts of the CNS separated by a period of at least one month, and each lasting a minimum of 24 hours. She also meets McDonald 2005 Criteria: 2 demonstrates two or more attacks and objective clinical evidence of two or more lesions (shows dissemination in space: two or more MRI-detected lesions consistent with MS, dissemination in time: two separate clinical attacks). Her initial MRI also met the 2005 criteria for lesion dissemination in space (3 of: (i) >9 T2 lesions, >3 periventricular lesions, >1 juxtacortical lesion or (iv) >1 infratentorial lesion). As well, her baseline MRI also met the newer

Figure 1: Axial and sagital T2 FLAIR images showing periventricular, corpus callosal, and juxtacortical white matter lesions.
McDonald 2010 Criteria:3 dissemination in space (>1 T2 lesion in at least 2 of 4 areas of CNS (periventricular, juxtacortical, infratentorial, spinal cord)) and dissemination in time (simultaneous presence of asymptomatic gadolinium-enhancing and nonenhancing lesions). CSF oligoclonal bands were present – a finding noted in 92% of pediatric MS patients.4 Investigations excluded other conditions. Thus, by all criteria, she has a diagnosis of MS. Pediatric MS represents up to 10% of all cases and is characterized by a relapsing-remitting course (RRMS).

SHOULD TREATMENT BE INITIATED?

This decision can be made based on predictors of poor outcome in MS, as well as the natural history of the untreated disease. Based on data from RRMS in adults (as limited studies have been done in children), it has been found that early disease outcomes such as a) incomplete recovery from first attack and b) shorter time to second attack are strong predictors of poor prognosis and future disability (reviewed in 5), both of which this patient exhibits. The natural course of RRMS, if untreated, is as follows: in 10 years, 30-50% of patients require walking aids, and in 30 years, up to 80% require walking aids, and up to 30% are restricted to their bed with effective use of only their arms.6 Due to the certainty of her diagnosis, and likelihood of future disability, this patient would be counseled to consider treatment.

CHOICES FOR LONG TERM TREATMENT

Currently there is no cure for MS. Long-term treatment encompasses first and second-line therapies (reviewed in 7, 8).

First line therapy: Immuno modulation

First line therapy for MS includes interferon β (Rebif, Avonex, Betaseron) and glatiramer acetate (Copaxone). The clinical benefit of interferon β is thought to be mediated through several mechanisms: inhibition of proinflammatory cytokines, induction of anti-inflammatory mediators, reduction of lymphocyte migration across the blood brain barrier, and inhibition of T-cell activation, among others. In Phase III pivotal trials in adult MS, interferon treatment demonstrated a 30% reduction in relapse rate compared with placebo for periods of 2-3 years.7 Formal trials have yet to include patients under 18 years old, but retrospective reviews show benefit and suggest safety and tolerability (reviewed in 7, 8).

Glatiramer acetate is an acetate salt mixture of synthetic polypeptides designed to mimic human myelin basic protein (MBP). It is postulated to induce regulatory and/or suppressor T cells, shift T helper response from Th1 to Th2, and shift antigen presenting cell function to type II. It was found to reduce number of relapses by 29% in adults with RRMS over 2 years.8 Studies in children are limited but it seems to be effective (reviewed in 8).

First-line treatment failure can occur due to inadequate effectiveness (failure to reduce relapse rate), intolerable adverse effects or presence of unacceptable level of breakthrough disease (severity or frequency of attacks).9 It is difficult to define treatment failure and consensus criteria for children have not been established. However, one paper showed that 1/4 of children experience breakthrough disease and switched to second-line therapy an average of 1.5 years after starting first-line therapy.10

Second line therapy

Second line MS therapy includes cyclophosphamide and natalizumab. Cyclophosphamide acts to induce a general state of immunosuppression. Its mechanism is presumably through lymphocytoxicity and decreasing lymphocyte subsets (reviewed in 8). It is used in adult patients with severe active MS, and a retrospective study in pediatric patients with severe MS revealed a reduction in the mean annualized relapse rate, although 75% of patients acquired new lesions on MRI over 12-24 months of treatment.11 The risk of infertility, infection and long-term malignancy increases with total dose and strategies for fertility preservation should be considered (reviewed in 8). It is an option for aggressive MS refractory to first-line therapies.

Natalizumab (Tysabri) inhibits VLA4 through binding to a subunit of α4β integrin, inhibiting lymphocyte migration across blood brain barrier and also resulting in T-cell apoptosis. In adult MS trials, it has been shown to decrease relapse rates by 68% and reduce the formation of new enhancing lesions by >90% relative to placebo.12 Open label case series in adolescents described a marked relapse-rate reduction and favorable safety profile (reviewed in 8). However, it has been associated with increased risk of opportunistic infection. Of particular concern, Tysabri has been associated with a 1/1000 incidence of active infection with JC virus, leading to progressive multifocal leukoencephalopathy (PML), an infection almost exclusively associated with immunosuppressed patients including AIDS. Careful monitoring strategies including prior determination of JC virus serology are now in place and protocols for treatment of PML are being optimized (reviewed in 14). Nonetheless, PML is a major deterrent for widespread use of Tysabri.

TWO MODELS OF CARE

The nature of MS as a chronic disease and its onset in childhood lend careful consideration to the intensity of initial therapy. Two potential models of care (as discussed in 8) can be considered: 1) ‘Start low and escalate if necessary’ and 2) ‘Start strong and maintain.’ Approach #1 is currently the standard of practice for most pediatric MS patients. It emphasizes greater safety with reduced potency and may be valuable to consider in multiple sclerosis, a disease with lifelong exposure to medication. Approach #2 involves powerful immunosuppression followed by maintenance of remission by less potent medications, which is similar to care of pediatric patients with severe rheumatological disease. It is considered for newer therapies and more aggressive disease, as it provides greater early disease suppression, which is important to consider in the context of limiting inflammation-mediated brain injury in the context of a developing pediatric CNS. However, it carries greater risk of toxicity, significant risk of opportunistic infection (e.g. PML in the case of Tysabri) and consideration of potentially life-altering decisions (e.g. fertility implications in the case of cyclophosphamide), which is especially pertinent in the care of pediatric patients. In this case of our patient: should the treatment decision reflect the current standard of care for pediatric MS patients or does her highly aggressive disease indicate that second line therapy should be pursued?

EPILOGUE

The family decided to pursue cyclophosphamide as their choice of treatment. Though the role of the physician is to guide patients and their families towards appropriate treatment, it is pertinent to keep in mind that the family has the final decision.
REFERENCES


Nodular regenerative hyperplasia of the liver presenting with ascites in a woman with limited systemic sclerosis

Arielle Mendel (Meds 2013)
Faculty Reviewer: Dr. Lori Albert MD, FRCPC (Division of Rheumatology, Toronto Western Hospital, University of Toronto)

CASE

A 57-year old Caucasian female was being followed for a 30-year history of limited systemic sclerosis. Her disease first presented with Raynaud’s phenomenon in 1980, and she subsequently developed digital calcinosis, dysphagia and esophageal reflux, sclerodactyly, and widespread telangiectasia.

In 2003, she developed progressive dyspnea on exertion accompanied by chest tightness and a single episode of syncope. Physical examination was significant for a split S2 with a loud pulmonic component. Pulmonary function testing showed a decreased diffusion capacity. RVSP was found to be elevated on 2D-Echocardiogram. These findings supported a diagnosis of pulmonary arterial hypertension (PAH) secondary to scleroderma. She received continuous IV prostacyclin infusion in combination with an oral prostacyclin analogue. Sildenafil was added in 2007, due to worsening exercise tolerance. She underwent evaluation for lung transplantation, but a decision was reached to defer the procedure unless her status worsened further.

In 2007, the patient began to experience intermittent episodes of dull and diffuse RUQ pain. Her abdomen was noted to be protuberant on several occasions. However, repeated laboratory tests and imaging of abdomen and liver remained normal. An upper GI endoscopy was performed in 2008 and showed no significant abnormalities.

In June of 2011 she presented to the ER with increasing RUQ pain, abdominal fullness, and weight gain of 10 lbs despite decreasing appetite over the last 2-3 months. There was no icterus or pedal edema. AST and ALP were mildly elevated (45 IU/L and 161 IU/L respectively), with normal albumin and INR. Abdominal ultrasound showed ascites, splenomegaly and bilateral pleural effusions, and she was admitted to hospital for further evaluation. Paracentesis revealed a serum-to-ascites albumin gradient of 11 with no evidence of infection. Hepatic venous pressure gradient was at the upper limit of normal (5 mmHg). Gastroscopy showed marked portal hypertensive gastropathy with no significant varices. Cardiac RVSP was measured at 96 mmHg (N<40 mmHg) on 2D-echocardiogram, which had remained stable at this level for the past few years.

A transjugular liver needle biopsy was then performed. This revealed loss of small portal veins and nodularity of the hepatic parenchyma with minimal fibrosis, no fibrous septa and no evidence of cirrhosis or other disease. Of note, bile ducts were present in normal numbers and appeared normal, with no observed cholestasis. These histological changes were diagnostic for Nodular Regenerative Hyperplasia (NRH) of the liver.

The treating physicians felt that this patient’s presentation of RUQ pain with ascites was the result of non-cirrhotic portal hypertension secondary to NRH, which was further exacerbated by severe PAH. The patient was treated with gentle diuresis and supportive management, and over the course of her admission her ascites diminished moderately and pleural effusions resolved. It was recognized that aggressive diuresis, therapeutic paracentesis or a transjugular intrahepatic portosystemic shunt (TIPS) procedure were all contraindicated given her fragile cardio-pulmonary status secondary to PAH. She was discharged after two weeks on spironolactone, a no added salt diet, and continued close monitoring of fluid balance. Unfortunately, this complication of her disease will limit her suitability for future lung transplantation.

DISCUSSION

Systemic sclerosis (SSc) or scleroderma is a rare disease characterized by progressive fibrosis of cutaneous, vascular and/or visceral connective tissue.\(^1\) The pathogenesis is linked to sustained immune-mediated activation of fibroblasts and endothelial cells.\(^2\) The ‘limited’ or ‘diffuse’ subtypes of SSc differ with respect to the extent of skin fibrosis, organ involvement, antibody production, and survival.\(^1,3\) Features of limited SSc (l-SSc) include the CREST syndrome (calcinosis cutis, Raynaud’s phenomenon, esophageal dysmotility, sclerodactyly, telangiectasia) and anti-centromere antibodies.\(^4\) Patients with either subtype require continuous monitoring for specific organ complications, and supportive treatment targeted towards affected tissues.

Nodular regenerative hyperplasia (NRH) is a pathological description for abnormal regenerative nodules within the hepatic parenchyma in the absence of fibrosis.\(^5\) NRH is a rare diagnosis, known to develop in the context of autoimmune, hematologic and malignant disorders as well as certain drug exposures.\(^5\) In a case series of 42 patients with NRH, one quarter had an underlying rheumatologic disorder\(^6\), and a recent review found 7 reports of NRH associated with SSc or CREST syndrome.\(^5\)

The regenerative nodules in NRH are thought to be a reactive process of hepatocytes secondary to disrupted vascular flow.\(^5\) Clinically, NRH belongs to a heterogeneous group of disorders causing non-cirrhotic portal hypertension, characterized by elevated portal pressures, ascites, or varices in the absence of cirrhosis or significant liver dysfunction.\(^1,5,8\) The pathogenesis of non-cirrhotic portal hypertension likely involves pre-sinusoidal and portal vessel injury, fibrosis, and thrombosis.\(^5,7\) The chronic inflammation, auto-antibodies, and pro-thrombotic state present in rheumatic diseases may precipitate this process.\(^6,8\) In SSc, the abnormal fibroblast activity responsible for cutaneous thickening may also be present in...
the portal tracts.10

Although non-specific liver abnormalities are common in SSc,11 intrinsic liver disease is seen infrequently.12 Primary Biliary Cirrhosis (PBC), involving progressive obliteration and fibrosis of intrahepatic bile ducts, is the liver disease most commonly associated with l-SSc.3,4,15 Conversely, NRH is a very rare complication16,17, and only case reports exist in the literature.1 Interestingly, NRH has been reported as an overlap syndrome with PBC in patients with CREST.15,16 In this patient, a minimally elevated ALP in the presence of normal bile ducts in the biopsy specimen makes a diagnosis of overlapping PBC unlikely.15

NRH should be considered in the context of preserved liver function, minimally elevated liver enzymes, and no evidence of cirrhosis.9 The diagnostic gold standard for NRH is liver biopsy14; imaging and other non-invasive tests are less helpful diagnostically.5,17 Management consists of treating the underlying condition(s) and preventing or treating portal hypertension, as these are the main prognostic factors in this condition.5,16

Portal hypertension will eventually develop in 50% of patients with NRH, but it is uncommon for manifestations such as ascites to be present at the time of diagnosis.6,15 One of the factors that likely contributed to this patient’s dramatic presentation was her long-standing pulmonary arterial hypertension (PAH), which is estimated to affect 10-25% of SSc patients.18 Prostacyclin analogues, endothelin-receptor antagonists and PDE-5 inhibitors have been shown to improve function and delay progression in patients with PAH-SSc.19,20,21, but it remains the leading cause of mortality in patients with l-SSc.18 Interestingly, there have been numerous reports of NRH co-existing with PAH in patients with SSc and other diseases, suggesting that a common vascular pathogenesis may underlie these conditions.5,15,21,22 Alternatively, PAH may be responsible for producing the circulatory disturbance that initiates the development of NRH.23

This is an example of a rare condition, Nodular Regenerative Hyperplasia of the Liver, presenting in a relatively rare disease, scleroderma. The initially subtle signs and lack of laboratory abnormalities further confounded efforts to identify the underlying problem. Our patient had a prolonged stay in hospital, and the ability to make the diagnosis and provide appropriate care required the collaboration with, and expertise of hepatologists, gastroenterologists and respirologists. This case highlights the need for multidisciplinary management of patients with complex rheumatic disorder, particularly in the setting of diagnostic and therapeutic dilemmas. Further research is warranted to investigate the relationship between pulmonary hypertension and the vascular pathogenesis of NRH.

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Gastric Schwannoma: a rare Schwann cell tumour of the GI tract

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Schwannomas are benign, slow-growing, encapsulated nerve-sheath tumors arising from Schwann cells, which are responsible for the myelin sheath in the peripheral nervous system. Schwannomas are most commonly found in the cranial vault, involving the myelin-forming cells of the 8th cranial nerve, in a condition called vestibular neurona. In rare cases, they can also occur in the GI tract, usually in the stomach. GI schwannomas are often non-encapsulated, but well demarcated.

Gastric schwannomas account for only 0.2% of all gastric tumors and 4% of all benign gastric neoplasms. The peak incidence is in the 4th and 5th decade of life, usually involving females. They can also occur in children, and can be malignant in rare cases. The majority of patients have remained asymptomatic for extended periods of time, with most cases discovered incidentally on imaging or laparotomy. Symptomatic patients most often present with ulcerations and upper GI bleeding, and a palpable mass may be present if the tumor grows exophytically. Malignant transformations are exceedingly rare, but have been reported.

CASE

The patient is a 34-year-old female who presented to the ER with RLQ pain and lower back pain persisting for the past 10 days. Her vital signs were stable with a normal white cell count.

CT-scan of her abdomen showed a normal appearing appendix. Fluid was seen in the pelvis, possibly secondary to a ruptured ovarian cyst. There was an incidental finding of a mass that appeared to be arising from the stomach. The mass appeared intramural and measured 5.1 cm x 4.4 cm. An ultrasound was done to look at lesions in the liver which were felt to be hemangiomas.

The patient’s pain was somewhat controlled with morphine, although it was still present. No cause of pain was determined. She was discharged from the emergency department with Percocet and scheduled to return for an esophagogastroduodenoscopy (EGD) approximately 4 weeks later.

Upon return for the EGD, the patient’s pain was much improved and she discontinued all her pain medications. The EGD showed a submucosal mass 5 cm below the gastroesophageal junction. The patient was referred to GI to for endoscopic ultrasound (EUS).

When seen by GI one month later, the patient revealed a prior history of anxiety disorder and was being treated with Paxil. She also had constitutional symptoms of anorexia and reported a 45-pound weight loss. An upper endoscopy was performed and the gastric mass was visualized along the lesser curvature of the stomach. The mass felt firm when probed.

On endoscopic ultrasound, the mass appeared hypoechoic but had evidence of hyperechogenicity foci. It measured 5.2 cm x 3.3 cm in its largest dimensions and was well demarcated, originating from the muscularis propria of the stomach. There was evidence of a perigastric lymph node as well as two celiac lymph nodes. A fine needle aspiration (FNA) for cytology as well as a core biopsy for histopathology was performed on the primary mass and one of the nodes. The mass was not endoscopically resectable.

Microscopic evaluation of lesion cells revealed a palisaded growth configuration, with elongated spindled nuclei and pointed ends. No mitosis or necrosis was seen. Immunohistochemistry was positive for S-100; negative for CD117, CD34, desmin, muscle specific actin and caldesmon. These findings were consistent with a diagnosis of schwannoma.

An ultrasound was done approximately 6 months later to reassess the mass, which appeared unchanged. She is currently being followed with annual CT-scans; no surgery is planned.

DISCUSSION

This is an interesting case of a gastric mass found incidentally for the presentation of right lower quadrant pain.

Briefly, the presenting pain was relatively severe and never explained. Appendicitis is the most likely cause of acute RLQ pain, but our patients’ appendix appeared normal on CT-scan. There was also suspicion of a ruptured ovarian cyst based on fluid seen in the pelvis on ultrasound. However, the ovaries were normal and this
diagnosis was somewhat inconsistent with the patient’s 10-day history of pain: fluid from an uncomplicated ruptured ovarian cyst is normally reabsorbed in 24 hours, with the pain resolving in a few days.\textsuperscript{11} The pain did resolve, and further investigations focused on the incidental gastric mass.

The differential diagnosis of a submucosal gastric mass is broad and includes gastrointestinal stromal tumor (GIST), leiomyoma, leiomyosarcoma, and schwannoma, among others.\textsuperscript{12} Upper endoscopy is useful in examining epithelial tumors; however, it is inadequate for examining tumors below the mucosa.\textsuperscript{13} In contrast, EUS is effective in visualizing submucosal tissue adjacent to the gastric wall and can be used to precisely guide needle biopsies.\textsuperscript{15}

It is important to differentiate between gastric schwannomas and other mesenchymal tumors, particularly the main differential of GIST, which has a higher chance of being malignant. The diagnosis of a GIST would mandate surgical resection if possible. Imatinib is used both as an adjuvant therapy when the GIST is completely excised and palliatively for unresectable or metastatic disease.\textsuperscript{1,2,4,5} It was found that virtually all cases of GIST would exhibit malignant behavior if followed, and metastatic cases can be effectively treated with imatinib mesylate, which improves survival from <50\% to >90\% at 1 year.\textsuperscript{14,15} In comparison, schwannomas remain benign in nearly all cases, and are rarely symptomatic.\textsuperscript{5} As the tumor enlarges, it displaces the nerve to the periphery, preserving its function.\textsuperscript{16}

Symptoms can result from the enlarging submucosal tumor restricting circulation to the mucosa, leaving it ischemic and prone to ulceration, bleeding, and damage by gastric acidity.\textsuperscript{17}

Imaging modalities such as CT, ultrasound, and MRI can provide limited but useful information. Schwannomas often appear uniform on CT, which can distinguish it from leiomyomas and leiomyosarcomas; ultrasound with a sufficient resolution can determine the tumor’s layers of origin, and MRI can map the precise location of the tumor and the displacement of its surrounding organs.\textsuperscript{18,19,20} These findings may also be helpful in explaining the cause of symptoms as well as determining the best approach to treatment, particularly in surgical cases.

Due to the similar spindle-shaped appearance of schwannomas and other gastric mesenchymal tumors, it can be difficult to distinguish between them using light microscopy.\textsuperscript{21} Grossly, they resemble leiomyomas and other stromal tumors: solitary, firm, smooth, white- and redish in color, and well circumscribed.\textsuperscript{5} Advances in immunohistochemistry allowed for a more precise differentiation: in one study, 24 out of 306 gastric spindle-cell tumors were diagnosed as schwannomas using immunohistochemistry, but only 9 were diagnosed as schwannomas using hematoxylin-eosin.\textsuperscript{22}

Immunohistochemical diagnosis of schwannoma is based on positivity for the S-100 protein, and negativity for CD117, CD34, desmin, and muscle specific actin.\textsuperscript{23} CD117 and CD34 are positive in GIST, and muscle specific proteins such as actin, desmin, and caldesmon are positive in smooth muscle tumors such as leiomyoma and leiomyosarcoma; all of which are negative in schwannomas.\textsuperscript{23} Our patient’s results are congruent with this guideline and a definitive diagnosis of schwannoma can be made.

Surgical treatment for gastric schwannomas would involve complete resection of the tumor.\textsuperscript{24} For our patient, this would mean a gastrectomy: the complete or partial excision of the stomach. The post-operative prognosis is excellent\textsuperscript{5,3} and most patients return to their pre-operative quality of life.\textsuperscript{25,26} However, it is debatable whether or not surgery should be deemed necessary for benign, asymptomatic schwannoma patients. In our opinion, surgery should be reserved for either malignancy or for symptomatic cases, especially for difficult operations such as in our patient. Most of the literature on surgical outcome appears to be based on cases were diagnosed as schwannomas post-operatively; therefore, the benefits of surgery for known asymptomatic cases are unclear.

Taking into account the available information, we felt that it was best to follow our patient with annual CT-scans, and to defer any surgical intervention until her symptoms become unmanageable; or until the improbable event that her tumor becomes malignant.

\textbf{REFERENCES}


Diabetic Foot Syndrome in a Middle Aged Male with Complicated Type II Diabetes

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Faculty Reviewer: Dr. Heather Percival MD, CCFP (Department of Family Medicine, Seaforth Community Hospital)

Diabetes mellitus (Diabetes) represents a group of metabolic disorders characterized by elevated plasma glucose levels and abnormal insulin activity within the body. Diabetes can be further classified into Type 1 (T1DM) and Type 2 (T2DM). T1DM is caused by an autoimmune failure of the beta cells in the pancreas leading to the complete absence of insulin in the body. In T2DM, hyperglycemia stems from a combination of insulin resistance, insulin deficiency and abnormal glucagon synthesis.\(^1\)

The number of individuals with diabetes has been increasing at an alarming rate. In 2000, the worldwide prevalence of diabetes was estimated to be over 150 million. It is projected that in 2025 this number will reach 380 million.\(^2\) Within Canada, it is projected that 2.4 million Canadians will have diabetes by the year 2016.\(^3\)

Diabetes is a serious condition that can lead to a wide variety of life threatening macrovascular (coronary artery disease, peripheral arterial disease, stroke) and microvascular (nephropathy, neuropathy, retinopathy) complications.\(^4\) The constellation of lower limb complications associated with diabetes such as ulcers and infections can be referred to as a diabetic foot syndrome (DFS).\(^5\) The following case will highlight the management of DFS with particular attention to diabetic foot infection.

**CASE**

Mr. D is a 41-year old resident of Southwestern Ontario who presented to a rural emergency department (ER) following a penetrating injury to the plantar surface of his left foot. The patient reported that he inadvertently stepped on a nail several days prior but failed to notice his foot had been injured. Mr. D denied any pain and disclosed that he has been diagnosed with T2DM for many years. In addition to the wound on the left foot, physical examination revealed the patient to be obese (BMI 44) with retinopathy, neuropathy, and a diabetic ulcer on the right foot. His current medications are: Metformin 1000 mg bid; Atacand 4 mg od; Losec 20 mg od; Lasix 40 mg od; Gabapentin 300 mg tid; Ditropan 5 mg bid; Vitamin D 1000iu od; Lantus insulin 51u hs; and Humalog 30u tid (adjusted +/- 2u). The ER physician cleaned the wound, confirmed a recent tetanus vaccination and prescribed Ciprofloxacin 500 mg bid with the explicit instructions for the patient to rest his foot.

One week following discharge, Mr. D re-presented to the ER, reporting that his left foot appeared worse. Physical examination revealed a grossly swollen, erythematous foot that felt warm to touch. The ER physician diagnosed Mr. D with an infected diabetic foot and performed an incision and drainage. A tissue specimen wound culture was obtained and grew mixed flora. The patient was admitted to hospital for IV antibiotics (Ciprofloxacin 500 mg bid and Clindamycin 600 mg tid) and strict bed rest. On admission the patient was afebrile with a WBC of 5.4 x10^9/L (normal 4-10). Following two days of treatment, the inflammation in Mr. D’s foot appeared markedly decreased and he was discharged from hospital on the third day. A follow-up physical exam by his primary care physician revealed the left foot to be completely absent of any signs of infection.

**DISCUSSION**

Foot infections are very common in patients with diabetes. Together with foot ulceration, foot infections have been identified as a major cause of morbidity and mortality in the diabetic patient as well as a major expense to health care systems.\(^6,7\) The propensity for diabetic patients to develop foot infections can be attributed to three pathological processes: neuropathy, vascular insufficiency and diminished neutrophil function.\(^8\) Patients displaying symptomatic peripheral neuropathy lose ability to sense pain in their lower extremities and thus fail to notice the presence of an abrasion, blister or penetrating trauma.\(^9\) In addition, the vascular insufficiency and diminished neutrophil function impairs the immune response.\(^10\) Together, these factors promote colonization of the wound by pathogenic organisms and the spread of infection from the surface to deeper tissue.\(^11\)

The diagnosis of diabetic foot infection is made clinically based on the presence of pus or at least two cardinal manifestations of inflammation (erythema, warmth, swelling or induration, and pain or tenderness). It is important to note that the presentation will vary from patient to patient. If peripheral neuropathy is present, the patient may report diminished or absent pain at the site of infection. Furthermore, 50% of diabetic patients with a significant foot infection will not have systemic signs of fever or leukocytosis due to a blunted cellular response to the infection.\(^11\)

Aggressive management of diabetic foot infections is crucial. Left untreated, these infections progress to gangrene and eventually require amputation of the limb. The wound should be cleaned, debrided and probed to identify sinus tracts, abscesses and the presence of osteomyelitis.\(^9\) Tissue specimens for wound culture should be obtained by scraping the base of the ulcer with a scalpel blade and processed for a Gram stained smear and aerobic/anaerobic cultures.\(^12\) Initial antibiotic therapy is empiric, broad spectrum and based on the severity of the infection. Severe infections require agents with coverage against Gram positive (including MRSA if necessary), Gram negative and anaerobic organisms. The patient should be evaluated for response to therapy in 1-3 days. If indicated by early culture results a modification to their antibiotic regimen can
Severe diabetic foot infections often require surgical management including incision and drainage, surgical debridement, revascularization and amputation. Following treatment, appropriate wound care is essential. Removing pressure from the wound, minimizing leg edema and maintaining a moist wound environment are all important factors that promote wound healing. Of all the diabetes related hospital admissions in North America, DFS accounts for 20%.

A focus on the prevention of DFS in diabetic patients will not only improve the quality of life of those patients but also help reduce the burden diabetic patients place on health care systems. It is recommended that diabetic patients engage in regular foot examinations. Higher risk individuals require foot care education regarding the avoidance of foot trauma, properly fitted footwear, smoking cessation strategies and optimization of glycemic control. Those who develop foot ulcers require management by multidisciplinary teams involving individuals specialized in diabetic foot care.

REFERENCES


A 19 year old with a bilateral posterior subcapsular cataract (PSCC) induced by corticosteroid cream

Abdul Naeem (Meds 2014)

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CASE

We present a case of a healthy 19 year old female on a three month follow-up to our clinic with a bilateral posterior sub-capsular cataract (PSCC) induced by a corticosteroid cream she used for one month due to her atopic dermatitis. All remaining medical history and systems review are normal. She is currently not on any medications. In her right (OD) eye her uncorrected vision (sc) is CF @ 4 ft, corrected vision (cc) is 20/40 and IOP is 12. In her left (OS) eye her uncorrected vision is 20/400, corrected vision (cc) is 20/70-2 and IOP is 13.

DISCUSSION

Cataract is the leading cause of blindness in the world.1 A cataract (from the Latin cataracta meaning waterfall) is defined as the clouding of the crystalline lens of the eyes. In normal healthy humans, the lens of the eye is usually clear whereas a person with cataracts may have a lens varying from slight to complete opacity. Until the fourth decade of life, the lens is able to change its shape. This allows the lens to focus on near and far away objects. The lens focuses the light rays on the back of the eye and the light signal is transmitted to the brain via the optic nerve.

In normal humans since embryonic development and onwards the lens of the eyes produce specialized cells that are arranged in a specific and complex orientation.2 These cells in the lens of the eye are stratified epithelia and contain large amounts of cytoplasmic proteins. These proteins are called crystallins and are transparent.2 However, the lens are unique in the sense that they “do not shed nonviable cells”3 and so the “lens is susceptible to degenerative effects of aging on cell structure”5. And so subsequently with advanced aging of the lens, the lens becomes cloudy. This cloudiness or cataract can then obstruct the passage of light and in effect cause deviation from normal vision.

Factors that may lead to cataract formation are: advanced age, smoking, alcohol consumption, poor lifestyle habits (including malnutrition and physical inactivity), long-term exposure to ultraviolet light or radiation, congenital factors, surgical complications, corticosteroid drugs, and secondary effects of diseases such as diabetes, hypertension and trauma.4,5

In the case presented, the cause of cataracts was eye exposure to a corticosteroid cream used for atopic dermatitis. Corticosteroids are heavily used for treating localized and systemic inflammatory conditions in dermatology. The administration methods are usually topical, oral or inhaled. Corticosteroids affect a large spectrum of bodily systems and specifically may result in an early forming cataract and an increase in intra-ocular pressure (IOP), which is a risk factor for Glaucoma. With this in mind, corticosteroids should be prescribed with time spent on patient education and possible treatment complications.

The patient presented in this case was monitored for IOP, which was noted as stable and normal. However, she did develop a sub-capsular cataract, which is formed in the posterior portion of the lens. This type of cataract is “particularly visually disabling”6 as it is formed “nearest to the eye’s focusing or nodal point”.6 In terms of corticosteroid administration, “topical steroids have the most effect nearest to the eye’s focusing or nodal point”.6 There is some research also suggesting that inhaled corticosteroids may lead to cataract formation as well.

In conclusion, though cataracts can be quite disabling and can significantly affect the quality of life of a patient, they do not damage the eye. With the technological advances in cataract surgery, cataract extraction can be successfully managed with an outpatient procedure.7,8 Patients are usually seeing a lot better within 24 hours.

Considerations for surgery, risk factors, and options for intra-ocular lens, were discussed with our patient. In this case, the patient still had quite a bit of manageable vision and decided to watch and wait for now. A follow-up of 6 months was scheduled when her eyes will be reassessed and operated on if she agrees and meets the surgical indications. Indications for surgery would include difficulty with routine daily activities of living, school or driving.

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