A Retrospective Descriptive Study of Stat TPN Orders in the Neonatal Intensive Care Unit

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Abstract

Background. Total parenteral nutrition (TPN) is used in the Neonatal Intensive Care Unit (NICU) to meet metabolic demand and provide growth. To prevent harm from critical laboratory abnormalities, stat TPNs can be ordered urgently to change the content of infusing TPN. Each stat order breaks the daily cycle and often leads to additional stat orders. Limited supplies of ingredients brought focus on our liberal stat TPN policy and how to reduce the number of stat TPNs safely. The purpose of this project was to evaluate biochemical abnormalities associated with stat TPNs and identify leverage points to reduce stat TPNs in NICU patients.

Methods. Data from 1/1/10 to 6/30/10 were abstracted from Meditech, NeoData, and patient charts for NICU stat TPN orders. Demographics, laboratory results (sodium, potassium, calcium, and glucose), and key variables were gathered and critical laboratory values were identified.

Results. A total of 112 patients had evaluable orders for 255 stat TPNs. Mean gestation was 31 weeks (SD = 5) and birth weight was 1.744 kg (SD = 0.993). Seven (3%) were never infused. Twenty (12.6%) of first stat TPNs were from patients taking nothing by mouth. Eighty-eight of first stat TPNs had no critical labs (55% of initial stat TPNs). Of follow-up stat orders, 43% (38/89) followed unnecessary initial stat TPNs. Of the 55 abnormalities that generated the initial stat TPNs, 44 (80%) corrected.

Conclusions. Fifty-two percent of stat TPNs could not be justified. For situations that were justified, 20% of laboratory abnormalities from initial stat TPNs were not corrected. These data provide an opportunity to reduce unnecessary costs and save limited resources.

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Introduction

Total parenteral nutrition (TPN) is the intravenous infusion of all nutrients necessary to meet metabolic demand and provide growth.[1] It is used commonly in the Neonatal Intensive Care Unit (NICU) and has shortened hospital stays and improved outcomes of neonates over the past four decades.[2] Because TPN bypasses enteral filtration and regulation, patients on TPN require close monitoring of laboratory data[1] to prevent complications such as seizures, apnea, poor tone, and fatal arrhythmias.[3]

Electrolyte abnormalities can be corrected with manipulations to the content of the TPN, changing the sources of fluids or by changing the rate of delivery of the existing TPN. Changes in the content of TPN usually are accomplished through the writing of a daily order, however, many NICUs have the option to use a stat TPN order. To date, there have been no studies on the factors driving stat TPN orders.

A new TPN order is written during morning rounds in our hospital. The order is prepared in the afternoon and hung for infusion around 1800. If the content of the TPN needs to be changed later in the day based upon a change in a patient's nutritional requirements, concerns for necrotizing enterocolitis, or electrolyte

abnormalities, a new TPN is written and labeled as stat. When a stat TPN is ordered, an additional TPN needs to be ordered later in the day to provide no gap in TPN coverage. Laboratory tests are repeated within 12 hours on infants with stat TPN orders to confirm correction of laboratory abnormalities or to identify additional required actions.

Opportunities for errors arise with each new stat TPN order. More than thirty steps with numerous safety checks are required to make each bag of TPN. In addition, it takes the time of two nurses and over 20 steps to hang each bag safely. Mistakes in any of the steps could lead to patient harm. Chances for infection are encountered with each stat TPN as the line needs to be broken and accessed to administer each new TPN. At our institution, the materials and labor costs associated with each stat TPN order is approximately $90.

Along with increased costs and risks associated with each stat TPN order, a shortage of key ingredients, such as cysteine and trace minerals, brought focus on our current ordering process. Our goal was to determine if and how we safely could reduce the number of stat TPN orders.

Methods

A list of all NICU stat TPN orders was obtained between January 1, 2010 and June 30, 2010 at Wesley Medical Center using Meditech, the electronic medical information system. Information was included about the composition of the existing TPN and/or enteral feeds, the composition of the stat TPN, the time the order was written, the time the TPN was hung, and the times laboratory data were drawn pre- and post-stat TPN order. Laboratory data most proximate to (both before and after) each stat TPN order were obtained. Demographic information also was collected from NeoData, the NICU medical records system. TPN infusion rates were verified by reviewing order sheets.

The first and follow-up stat TPNs were assessed separately. Subsequent stat TPNs were identified as any stat TPNs ordered within 48 hours of a preceding stat TPN. To classify abnormal laboratory data, two different cutoffs were used, “abnormal” as defined by the laboratory reporting system and “critical” as defined by the thresholds used in a recent clinical trial for serious adverse events.[4] (See Table 1).

Table 1. Cutoffs for laboratory data.

Laboratory Variable	Critical Low Values	Low Values	High Values	Critical High Values
Sodium (mmol/L)	130	135	148	150
Potassium (mmol/L)	3.0	3.5	6.0	6.5
Ionized Calcium (mg/dl)	4.0	4.5	5.3	6.5
Glucose (mg/dl)	45	60	125	175

Results

There were 112 patients who had stat TPNs written from January 1, 2010 to June 30, 2010. The mean birth weight of this population was 1.744 kg (+/- 0.993) and the mean gestational age at birth was 31 weeks (+/- 5). Sixty (54%) were males, 8 (7%) had necrotizing enterocolitis, and 14 (13%) had intraventricular hemorrhage. There were 259 total stat TPNs during the study period. Four stat TPNs were unevaluable because of insufficient data. Seven stat TPNs were ordered but never hung.

First Stat TPNs. Of the remaining 248 stat TPNs, 159 first stat TPNs were identified. Twenty (13%) were for patients whose enteral feeds were stopped urgently and were taking nothing by mouth (i.e., NPO). Fifteen patients (9%) had no associated abnormal laboratory values, 73 (46%) had abnormal laboratory values that were not critical, and 51 (32%) had critical lab values. Of the 124 first stat TPNs with abnormal or critical laboratory values, 76 (61%) had one, 32 (26%) had two, 14 (11%) had three, and two (2%) had four. Of the 190 laboratory abnormalities, 55 (29%) were considered critical; an abnormality in glucose was the most frequent (40%).

Subsequent Stat TPNs. There were 89 subsequent stat TPNs. Forty-five (51%) followed stat TPNs with critical laboratory abnormalities and six (7%) were from patients that went NPO. Thirty-eight (43%) of these were written as follow-ups to stat TPNs that had non-critical or no laboratory abnormalities.

Impact of First Stat TPN. Pre- and post-laboratory data were compared to see whether the hanging of the stat TPN corrected the abnormality in the desired direction (see Table 2). Correction of critical labs with first stat TPNs failed to occur 20% of the time; hypo- and hypernatremia were most likely to fail to correct (36.4% non-correcting).

Table 2. Result of administering first stat TPN.

		Sodium	Potassium	Ion Calcium	Glucose
Critical Low Values	Correcting	8	2	1	19
	Total	13	2	1	20
Critical High Values	Correcting	6	4	2	2
	Total	9	4	3	3

Discussion

A liberal stat TPN policy leads to excessive costs, overuse of limited resources, and increases risks to patients. In this population, more than 43% of stat TPN orders were written because of abnormal but not critical laboratory values. In this scenario, other methods of correction, such as changing the rate of TPN or waiting to see if the abnormality would self-correct, could have been utilized. An additional 6% of all evaluable stat TPNs had no laboratory abnormalities and 3% of stat TPNs were written and made, but never hung. Therefore, more than half (133 of 255) of all evaluable stat TPN orders were not justified by patient condition or critical laboratory.

Even when stat TPNs were justified, there was room for improvement in the management of electrolyte and glucose abnormalities. Twenty percent of stat TPN orders failed to produce desired changes to critical laboratory data. Serum calcium and potassium were most likely and serum sodium was least likely to be corrected by

changes in TPN composition. This area should be studied further to find more effective ways to correct these biochemical abnormalities.

There were limitations to this retrospective study. Variables which may have influenced each stat TPN may not have been recorded or identified. Also, the percentages of abnormal laboratory values that would have self-corrected or been correctable using interventions other than stat TPN are not known. The flipside is that percentages of these abnormalities would have become critical without stat TPN also is not known.

No guidelines exist on when laboratory abnormalities warrant a stat TPN order. The implementation of a guideline in our environment for stat TPN orders would decrease the number of unnecessary first stat TPNs and their unnecessary subsequent stat TPNs. These guidelines could offer clinicians alternative methods for correcting subcritical laboratory abnormalities, which potentially could decrease costs and risks to our patient population.

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Keywords: neonates, total parenteral nutrition, neonatal intensive care, electrolyte balance

Treatment of Intractable Diabetic Macular Edema with Pegaptanib Versus Bevacizumab, Both in Combination with Dexamethasone

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Abstract

Background. Diabetic macular edema is a significant cause of vision loss, and some patients do not respond optimally to existing treatments. This study compared the response of intractable diabetic macular edema to intravitreal injection of two anti-VEGF drugs, bevacizumab and pegaptanib, both in combination with dexamethasone.

Methods. A retrospective chart review was conducted to examine patients from an ophthalmology practice in one year with diabetic macular edema (DME), recurrent or persistent, after focal laser or intravitreal bevacizumab. Patients received bevacizumab/dexamethasone or pegaptanib/dexamethasone. Outcome measures were improvement in best corrected visual activity (converted to LogMAR) and central macular thickness (CRT). Data on adverse effects also were collected.

Results. The bevacizumab/dexamethasone group included 25 eyes which had pre-treatment LogMAR = 0.69 ± 0.49 (mean ± SD) and CRT = 419 ± 131. Post-treatment LogMAR was 0.70 ± 0.48 and CRT = 377 ± 107. The pegaptanib/dexamethasone group included 14 eyes; pre-treatment LogMAR = 0.80 ± 0.55 and CRT = 520 ± 108. Post-treatment LogMAR was 0.77 ± 0.49 and CRT = 46 4 ± 106. Neither treatment had a significant effect on visual acuity. Both groups experienced a significant decrease in CRT over time (p = 0.006). The pegaptanib/ dexamethasone group had higher CRT at all times (p = 0.020), but the trend in CRT decrease was not different between the two groups. Intraocular pressure increased in both groups (p = 0.038). No other adverse effects were reported.

Conclusions. Neither bevacizumab/dexamethasone or pegaptanib/dexamethasone significantly improved visual acuity in intractable DME, but both decreased central macular thickness. Differences in outcome measures between the two treatment groups were not significant. The only adverse effect seen was a small increase in intraocular pressure.

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Introduction

Diabetic retinopathy occurs in approximately 29% of persons with diabetes mellitus and is severe enough to threaten vision among 4.4%.[1-3] Diabetic macular edema (DME) is a type of retinopathy resulting from microvascular damage to retinal capillaries, causing breakdown of the blood-retinal barrier and allowing leakage into the retina.[4-5] The resulting edema causes damage which can impair visual acuity and may result in blindness.[6-7] The prevalence of DME in diabetic patients varies from 0.9% to 29%.[8-10] Diabetic retinopathy is the leading cause of new onset blindness among Americans 20 to 74 years old[1] and accounts for 4.8% of blindness worldwide.[11]

Treatment for diabetic macular edema is complex, controversial, and changing. Laser photocoagulation with a focal/grid laser can decrease vision loss from DME,[12-14] however, a number of patients fail to respond optimally to laser treatment. Inflammatory processes may be an important component of retinal damage in DME,[15] which has led to investigation of intravitreal corticosteroids as a possible treatment.[16-18] Studies suggest intravitreal dexamethasone improves visual acuity and central macular thickness.[19,20] Adverse effects of intravitreal steroids include glaucoma and cataract formation.[21-22]

Vascular endothelial growth factor (VEGF) is another proposed culprit for damage in DME, possibly via increased vascular permeability and action as a pro-inflammatory mediator.[23,24]

Bevacizumab (Avastin®) is a recombinant humanized antibody that targets many VEGF isoforms.[25] Intravitreal bevacizumab is used off-label for DME.[26-31] Adverse effects of intravitreal bevacizumab include anterior chamber reactions from injection, increased intraocular pressure, endophthalmitis, and rare systemic effects.[27,32-34]

Pegaptanib (Macugen®) is a pegylated aptamer that binds and neutralizes primarily the 165-isomer of VEGF. It is approved for intravitreal use and is used off-label for DME.[35-37] Possible adverse effects of intravitreal pegaptanib treatment include endophthalmitis, retinal detachment, and traumatic cataracts.[38-40] Research has not determined the ideal treatment algorithm for diabetic macular edema and the role of anti-VEGF therapies.[41]

No studies have been published comparing the efficacy of bevacizumab and pegaptanib. These two anti-VEGF agents have slightly different structures and mechanisms of action and bevacizumab is significantly less expensive than pegaptanib. Additionally, no published studies have examined the efficacy of combination therapy with dexamethasone and anti-VEGF drugs. This study was designed to compare the efficacy of combined intravitreal treatments of pegaptanib/dexamethasone versus bevacizumab/dexamethasone for intractable DME.

Methods

Participants. A retrospective chart review was conducted to examine patients with DME in an ophthalmology practice who were treated during the 2010 calendar year with intravitreal bevacizumab/dexamethasone or pegaptanib/dexamethasone. Patients who were diagnosed with severe DME refractory to other treatments including focal laser therapy or intravitreal bevacizumab monotherapy had been offered combined treatment with intravitreal dexamethasone and an anti-VEGF agent.

Instrument. Inclusion criteria included a diagnosis of diabetic macular edema and an intravitreal injection of bevacizumab/dexamethasone or pegaptanib/dexamethasone. Patients who were lost to follow-up within five weeks of treatment were excluded. All eyes which met the inclusion/exclusion criteria were included in the analysis. The following data were collected from patient charts: best corrected visual acuity, central macular thickness measured by ocular coherence tomography (Cirrus HD OCT, Carl Zeiss Meditec, Jena, Germany), and intraocular pressure (Tono-Pen, Reichert Technologies, Depew, New York, USA). Data also were collected on patient demographics, duration of diabetes, and potential adverse effects of the treatment.

Method of Injections. After informed consent, patients were anesthetized with one drop of viscous lidocaine and two sets of proparacaine ophthalmic drops two minutes apart. One minute after the final anesthetic drop, subconjunctival injection of 2%

lidocaine with epinephrine was performed. The eye was prepared with topical 10% Betadine®, with application repeated after five minutes. Intravitreal injection was performed with one of the following agents: 1.25 mg bevacizumab, 0.03 mg pegaptanib, or 0.4 mg dexamethasone. Patients were instructed to use polymixin B/trimethoprim (Polytrim®) ophthalmic drops four times per day for three days before injections and one week following injections. Patients treated with combined therapy received dexamethasone and an anti-VEGF agent via the same procedure one to six weeks apart. Some patients received additional intravitreal treatments after the conclusion of data gathering, depending on response to treatment.

The clinical endpoints of this study were best corrected visual acuity (BCVA) and central macular thickness (CRT). Visual acuity was measured on the Snellen chart with the patient's current prescription and with a pinhole. When visual acuity improved significantly with the pinhole, this measurement was used as BCVA to decrease refractive error as a source of reduced visual acuity. BCVA was converted to the logarithm of the minimum angle of resolution (LogMAR) for analysis.[42] Central macular thickness (microns) was measured by ocular coherence tomography; this measurement has been shown to correlate with visual acuity and severity of retinopathy.[43] Change in intraocular pressure (IOP, measured in mmHg) from baseline to extended observation was calculated to evaluate a possible adverse effect of therapy. Data also were collected regarding other possible adverse effects from treatment, as well as diabetes history, patient demographics, and other ocular conditions.

Analysis. Data were collected on pre-treatment values, post-treatment values measured at the first visit after combined treatment (generally within several weeks), and extended observation values measured at the last visit of the year (an average of 4.5 months after initial treatment). Changes in clinical endpoints were assessed as the difference between the baseline measurement and the immediate post-treatment measurement. Baseline values for each variable were defined as the last measurement collected prior to intravitreal drug administration. Repeated measures multivariate analysis of variance (rMANOVA) was used to determine statistical significance after Mauchly's test of sphericity determined the appropriate statistical method.[44-46] A p-value less than 0.05 was considered significant.

This project was approved by the Human Subjects Committee at the University of Kansas School of Medicine-Wichita.

Results

In the 2010 calendar year, 25 eyes were treated with combined bevacizumab/ dexamethasone administered within a 6-week period (Table 1). There was large variability in this sample; the average pre-treatment LogMAR was 0.69 ± 0.49 (mean ± standard deviation) corresponding to an average visual acuity of 20/98, and average CRT was 419 ± 131 nm before treatment (Table 2). Initial post-treatment visual acuity improved in eight eyes (32%); decreased visual acuity was seen in seven eyes (28%), and 10 eyes (40%) experienced no change in visual acuity.

Pegaptanib/dexamethasone was used in 14 eyes (Table 1). Average pre-treatment LogMAR was 0.80 ± 0.55 corresponding to an average visual acuity of 20/126; pre-treatment CRT was 520 ± 108 (Table 2). Post-treatment visual acuity improved in five eyes (36%), four eyes (29%) experienced decreased visual acuity following treatment, and five eyes (36%) had no change in visual acuity.

Table 1. Bevacizumab and pegaptanib treatment groups.

	Number of Eyes	% Male	Mean Age (SD)	Mean Duration of Diabetes (SD)
Bevacizumab/dexamethasone	25	56%	68 ± 10	16 ± 11
Pegaptanib/dexamethasone	14	50%	70 ± 11	19 ± 9

Table 2. Values and changes in LogMAR (Logarithm of Minimum Angle of Resolution), Central Macular Thickness (CRT), and Intraocular Pressure (IOP).

	Pre-treatment (Mean ± SD)	Post-treatment (Mean ± SD)	Extended observation (Mean ± SD)	Mean Change in LogMAR (SD)	Mean Change in CRT (SD)	Mean Change in IOP (SD)
Bevacizumab/ dexamethasone	LogMAR: 0.69 ± 0.49 CRT: 419 ± 131	LogMAR: 0.70 ± 0.48 CRT: 377 ± 107	LogMAR: 0.70 ± 0.50 CRT: 391 ± 127	0.01 ± 0.22	-42 ± 96	0.2 ± 3.5
Pegaptanib/ dexamethasone	LogMAR: 0.80 ± 0.55 CRT: 520 ± 108	LogMAR: 0.77±0.49 CRT: 464 ± 106	LogMAR: 0.75 ± 0.50 CRT: 448 ± 133	-0.03 ± 0.17	-56 ± 85	3.2 ± 6.5
p-value				0.559	0.750	0.066

The pegaptanib group had increased baseline central macular thickness for patient age and diabetes duration (Figure 1). However, no trend was seen in the LogMAR data (Figure 2).

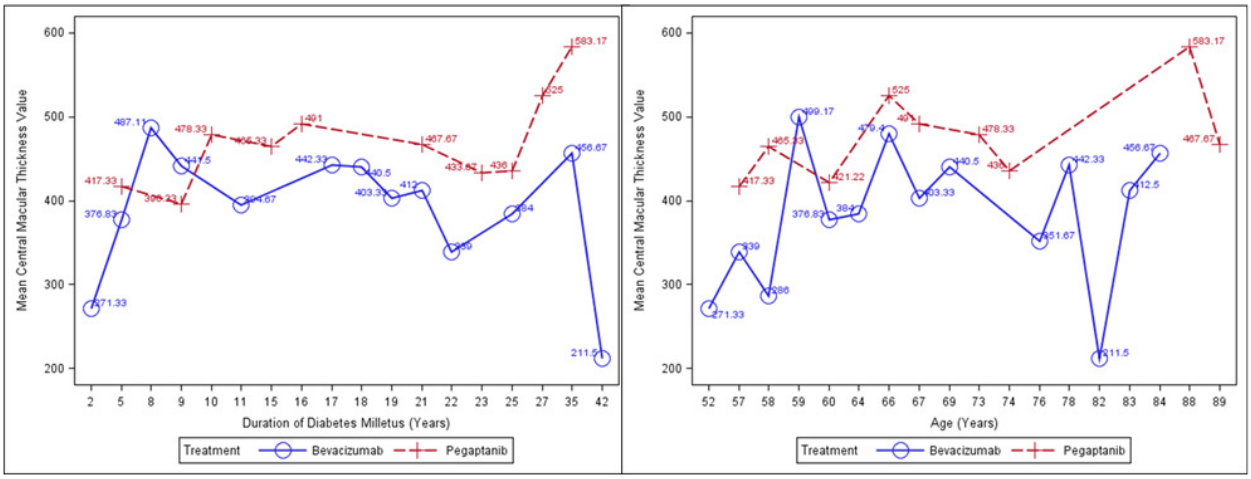

Figure 1. Graph of Central Macular Thickness over Age (right) and Diabetes Duration (left).

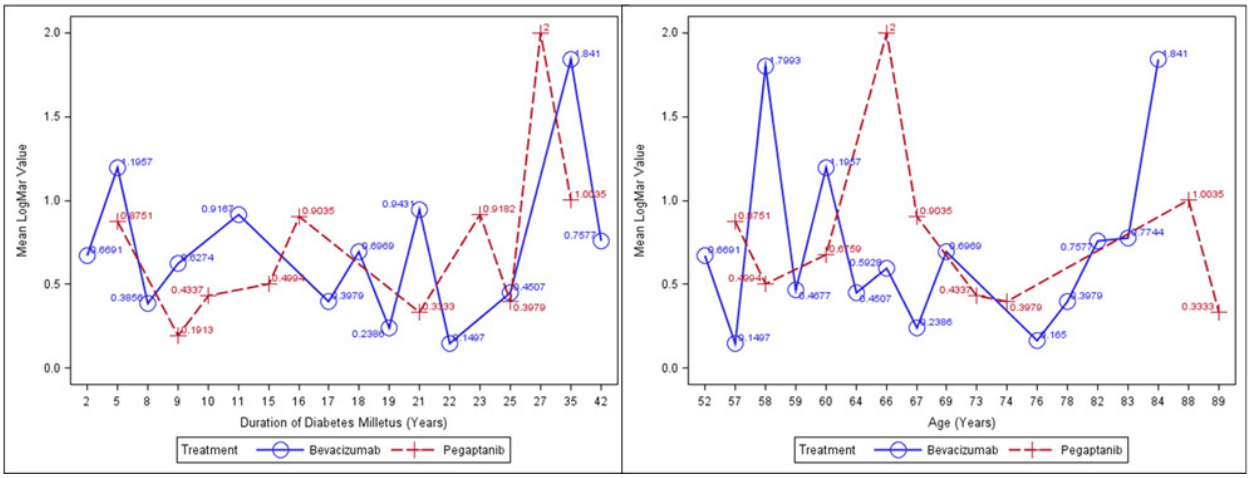

Figure 2. Graph of LogMAR over Age (right) and Diabetes Duration (left).

There were subtle differences between the LogMAR responses in the two treatment groups (Figure 3). Eyes in the pegaptanib group had worse baseline visual acuities and larger LogMAR values, but visual acuity improved over time. In contrast, visual acuity in the bevacizumab group remained relatively stable. However, these differences were not statistically significant. No statistically significant change in LogMAR between pre-treatment, post-treatment, and extended observation occurred in either group. Similarly, there were no differences between the pegaptanib/dexamethasone group and the bevacizumab/dexamethasone group averaged across all observations and over time.

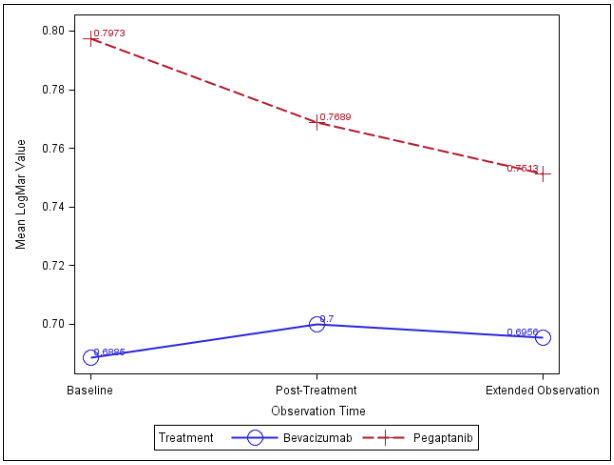

Figure 3. Graph of LogMAR over Time.

Both groups experienced a significant decrease in CRT over time (p = 0.006; Figure 4). At all observation points, CRT was higher in the pegaptanib group compared to the bevacizumab group (p = 0.020). However, the trends of the change in CRT were not significantly different for the bevacizumab and pegaptanib groups (reflected by the parallel lines in the figures). No significant change occurred between pre-treatment and post-treatment measurements or between post-treatment versus extended observation values.

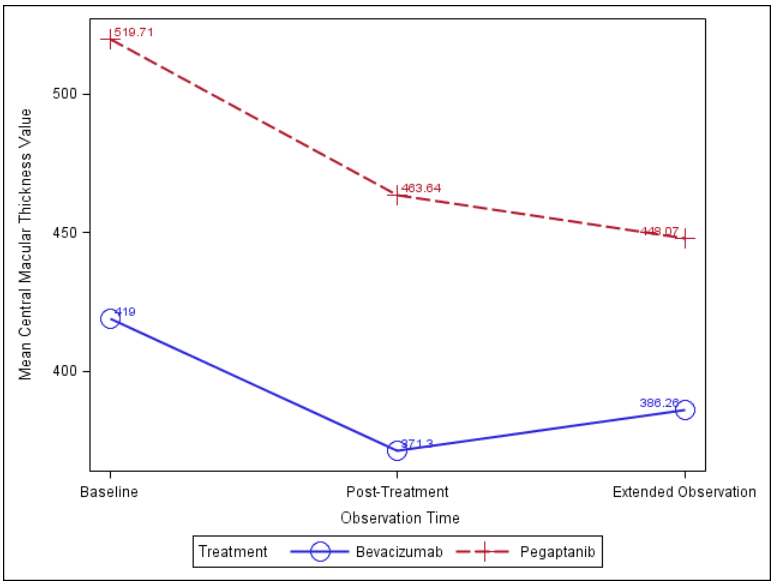

Figure 4. Central Macular Thickness over Time.

Intraocular pressure was measured at baseline and after extended observation to evaluate a possible adverse effect of therapy. A significant increase over time occured ($p = 0.038$; Figure 5). No patients in either treatment group received a new diagnosis of either intraocular hypertension or glaucoma during the course of this study. The pegaptanib group had a greater increase in IOP. The bevacizumab group maintained a more stable IOP, although the change was similar in trend and direction for the two treatment groups. There was no significant difference in IOP between the two groups when averaged over time.

Other than the increase in intraocular pressure, no other complications were reported for any of the eyes in this study. No ocular complications such infections or retinal detachment occured, and no systemic events such as myocardial infarction or cerebrovascular events were reported.

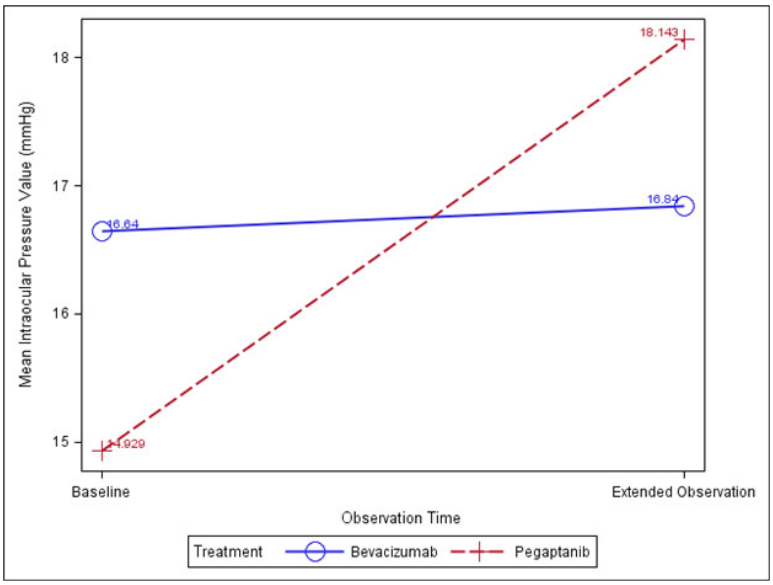

Figure 5. Graph of Intraocular Pressure over Time.

Discussion

There was no significant effect on visual acuity after treatment with either bevacizumab/dexamethasone or pegaptanib/ dexamethasone, and there was no difference in change in visual acuity and central macular thickness between the two treatment groups. Apparently, neither treatment is ideal for refractory diabetic macular edema and new therapies are needed to improve visual acuity. However, patients did not lose visual acuity during the study, so the treatments may have prevented further vision loss. This is difficult to assess in an uncontrolled study.

Significant decrease in central macular thickness occurred in both treatment groups. Persistent macular edema can lead to significant loss of vision in other ocular conditions.[47] It is possible that the same may hold true for DME, so the reduction in CRT could reduce risk of further retinal damage. Bevacizumab/dexamethasone and pegaptanib/dexamethasone worked equally well to decrease CRT. Although pegaptanib has more restricted anti-VEGF activity compared with bevacizumab (a nonspecific anti-VEGF agent), the two compounds had similar efficacy.

Previous studies have shown treatment with intravitreal bevacizumab improved visual acuity and central macular thickness in new-onset DME[30-31] as well as DME persistent after focal laser therapy.[26-28] Intravitreal pegaptanib also improves visual acuity and central macular thickness for DME[37] and new-onset DME specifically.[36] Our study suggested that the benefits of bevacizumab/dexamethasone and pegaptanib/dexamethasone are not as striking in patients with refractory diabetic macular edema who already have failed therapies such as intravitreal bevacizumab. Our study did not address the benefits of therapy in treatment-naïve patients.

The pegaptanib group had increased CRT for demographic variables and over time throughout this study. Although no trend was seen for visual acuity, higher CRT would be expected in more severe disease with increased edema. This may reflect a bias in treatment selection; patients with more severe DME may have been offered pegaptanib more frequently in attempt to preserve vision in DME refractory to other treatments such as bevacizumab monotherapy.

A small increase in intraocular pressure occurred in both the bevacizumab and pegaptanib treatment groups. No eyes in this study received a diagnosis of glaucoma or intraocular hypertension. Although the increase in intraocular pressure was statistically significant, it is not clear whether the small increase is clinically significant. The time of intraocular pressure measurement was not collected, and the normal diurnal variation in intraocular pressure could account for the change. Elevated intraocular pressure with resulting glaucoma has been reported as an important adverse effect of intravitreal steroid treatment with triamcinolone.[21-22] Our study suggested that dexamethasone may be less problematic than triamcinolone with regard to incidence of glaucoma. Further study on the long-term effects of treatment may clarify this issue.

Aside from the increase in intraocular pressure, no other ocular or systemic adverse effects were seen. There were no reports of endophthalmitis following intravitreal injection. This is noteworthy as there are reports of endophthalmitis following intravitreal bevacizumab, likely due to processing by compounding pharmacies.[32,33,48] While all data were collected from ophthalmology charts to evaluate adverse effects, complete health

records were not available. Data on systemic events may not have been available if events were not communicated to the ophthalmologist.

Limitations. This was a small retrospective pilot study with several inherent limitations. This study did not include a control group, and patients were not randomized into treatment groups. It may have been underpowered to detect subtle differences. Pertinent data were unavailable on many patients. For example, visual acuity was measured with a patient's current prescription but refraction was not optimized for the patient at the time of testing. Complete health records were not available, and background information on diabetes such as hemoglobin A_{1c} level was not recorded for many patients, limiting the ability to judge if the two treatment groups were initially equivalent.

Patients were treated with alternating injections of dexamethasone and an anti-VEGF agent. The influence of the steroid treatment may make it more difficult to compare pegaptanib to bevacizumab. This study examined patients over the course of one calendar year; extension of this study to examine a longer time frame would give a clearer picture of the duration of treatment effects as well as any adverse effects. This study was limited to patients with severe DME which previously had proved recurrent or refractory to therapy. These results cannot be generalized to draw conclusions about the benefit of bevacizumab, pegaptanib, or dexamethasone for new onset diabetic macular edema.

Conclusions

Patients with intractable diabetic macular edema did not experience significant improvement in visual acuity after therapy with bevacizumab/dexamethasone or pegaptanib/dexamethasone. However, decreased central macular thickness was seen after both therapies. There was no significant difference in outcome measures between the two treatment groups. Intraocular pressure increased slightly after treatment, but no other adverse effects were experienced by any eyes in this study.

Further study is needed to confirm these conclusions, ideally a large randomized, blinded, controlled trial to compare the efficacy of pegaptanib and bevacizumab. Study also is needed to examine the effects of these treatments for new-onset DME, to define the long-term effects of treatment, and to quantify the effects of dexamethasone when combined with either pegaptanib or bevacizumab. Research is needed on new therapies for refractory diabetic macular edema which would improve visual acuity as well as preventing further damage.

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Keywords: diabetic retinopathy, macular edema, pegaptanib, bevacizumab

Pentad's Triad: Revisiting Reynold's Pentad

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Introduction

Acute cholangitis is a potentially life-threatening complication of choledocholithiasis. It is defined as a triad of fever, jaundice, and right upper quadrant pain, also known as Charcot's Triad.[1] Sequelae of acute cholangitis includes suppurative cholangitis, known as Reynold's pentad. Reynold's pentad includes Charcot's Triad, hypotension, and altered mental status.[2] This report describes an unusual case of acute cholangitis in a patient who manifested three of the five findings of Reynold's pentad.

Case Report

An 88-year-old black woman presented with decreased oral intake, nausea, vomiting, and right upper quadrant pain that started two days prior to presentation. Her mental status was normal. The patient denied any history of fever, chills, or sweats. No change was reported in bowel movement in the form of diarrhea, melena, or hematochezia and no hematemesis occurred. She was afebrile and normotensive with initial blood work showing a bilirubin of 4.7 mg/dL with a predominance of conjugated (2.9 mg/dL) versus unconjugated (1.8 mg/dL). AST was 423 U/L, ALT 336 U/L, and alkaline phosphatase 271 U/L. The patient's white blood count was 11,800 cells/cmm. She also had a urinary tract infection.

A sonogram of the liver showed a 1.1 cm stone at the neck of the gallbladder without evidence of cholecystitis (Figure 1) and the common bile duct (CBD) was dilated up to 9 mm (Figure 2). She was started empirically on piperacillin/tazobactam for possible acute ascending cholangitis. A surgical consult resulted in a magnetic resonance cholangiopancreatography (MRCP) showing increased CBD dilatation to 1.4 cm. There was a 0.9 cm T2 hypointense focus at the ampulla of Vater, possibly representing a choledocholithiasis and a 0.9 cm stone at the gallbladder neck.

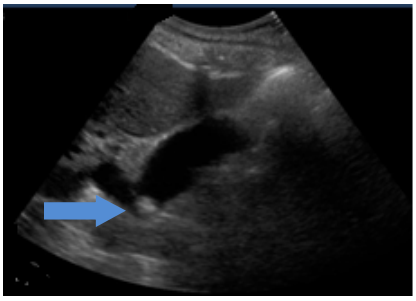

Figure 1. A 1.1 cm cholelithiasis at neck of gallbladder.

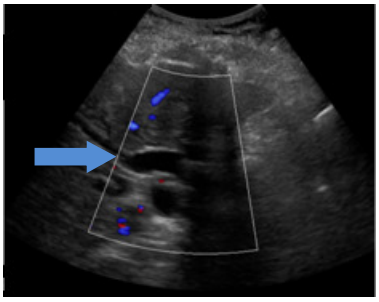

Figure 2. Common Bile Duct is 0.9 cm.

The patient had positive blood cultures growing gram-negative bacillus. The blood culture grew *Citrobacter freundii* which was susceptible to piperacillin/tazobactam. Within 25 hours of admission, her blood pressure dropped to 72/42 mmHg, requiring vasoconstrictors with norepinephrine and vasopressor, with a pulse of 102 bpm. The patient also developed worsening mental status and acute delirium.

A gastroenterologist was consulted and the patient was taken for urgent endoscopic retrograde cholangiopancreatography (ERCP) less than 36 hours after admission. ERCP showed a filling defect representing choledocholithiasis obstructing the distal aspect of the common bile duct (Figure 3). The INR was high (1.9) so a cholecystectomy was not recommended. She was on vasopressor and antibiotics. The decision was made to place a 7Fr 10 cm biliary stent without performing a sphincterotomy. Purulent drainage was seen upon stent deployment, followed by adequate bile flow (Figure 4). The next day, the patient's mental status returned to baseline. She had developed a leukocytosis of 20,000 cells/cmm. Her septic shock resolved off vasopressor agents and continued antibiotic therapy.

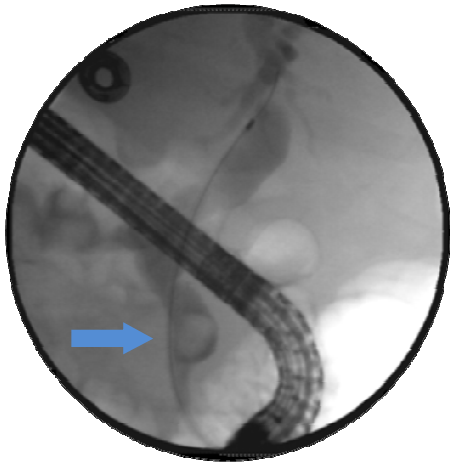

Figure 3. ERCP showing 9 mm choledocholithiasis at distal CBD.

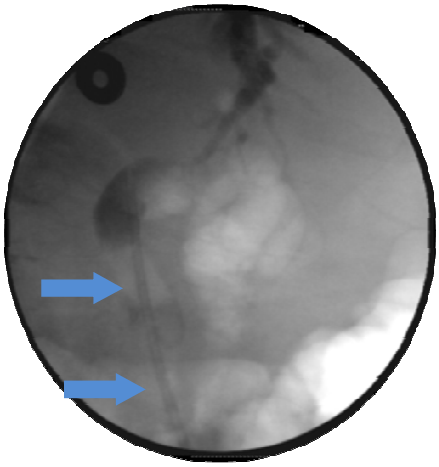

Figure 4. ERCP after stent placement bypassing choledocholithiasis at ampulla of Vater.

Discussion

This patient presented with acute cholangitis, which is a clinical diagnosis based on Charcot's Triad: fever, jaundice, and right upper quadrant pain.[1] Yet, our patient did not have fever or dermatologic evidence of jaundice, but she had icterus and a bilirubin level of 4.7mg/dL. Our patient was afebrile throughout her hospitalization. Interestingly, the elderly may not manifest fever during acute cholangitis.[3] Our patient's clinical course became complicated by hypotension with septic shock and decreased mental status with delirium, which suggested Reynold's pentad or suppurative cholangitis.[4,5] We labeled the presentation of signs and symptoms as Pentad's Triad because our patient truly manifested three of the five findings of Reynold's pentad. Suppurative cholangitis may be associated with increased mortality, especially in the elderly population.[6,7]

Treatment involves blood pressure support, antibiotic management, and endoscopic choledocholithiasis retrieval

with sphincterotomy or stent placement if stone retrieval and sphincterotomy is contra-indicated, such as in coagulopathies.[8-10] In case of the latter, a second attempt is made when the clinical acuity defervesce.

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Keywords: choledocholithiasis, cholangitis, case report

Early Recognition of Pulmonary Edema with OptiVol Fluid Index

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Introduction

Heart failure is the leading cause of hospital admissions for patients above 65 years and accounts for 3% of total national health care budget.[1] The largest share is due to hospitalization and re-hospitalization of these patients.[2] In-hospital mortality is 6.9% which increases to 10% in the following two to three months. One-year mortality is approximately 35% and there is a 24% risk of readmission.[3,4] One of the main reasons for morbidity and mortality is the absence of reliable markers for early recognition of decompensated heart failure and the lack of markers to check efficacy of long term treatments.[5] The methods used clinically for diagnosing heart failure (e.g., shortness of breath, exercise intolerance, weight gain, edema) are not reliable and may even be absent or not recognized in some patients.[6,7] Newer modalities of identifying fluid accumulation such as OptiVol fluid index have been useful in managing patients with heart failure.[8]

Congestive heart failure pathology is complex and involves severe hemodynamic and neurohumoral alterations.[3,8] In patients with diastolic and systolic heart failure, the increased left ventricular filling pressures can cause increased left atrial pressures and pulmonary edema from pulmonary venous congestion. These changes cause congestive symptoms. Hemodynamic alteration is a consistent finding and is the earliest change in the decompensation process. Increases in pulmonary pressure occur days to weeks before clinical symptoms are seen and may even persist after resolution of symptoms.[9,11,12] Measuring intrathoracic impedance by using an implantable device has been shown to be effective in early detection of heart failure and reduce hospitalization and mortality.[10] With this method, the impedance is measured between the coil of right ventricular lead and the defibrillator can. It uses a low level electric impulse that travels across the chest cavity and measures the resistance.[6] The measurement is made multiple times every day, as the fluid level increases intrathoracic impedance falls.[2]

The OptiVol index represents the difference between daily fluctuations and reference impedance (index increases as fluid accumulates).[7] The OptiVol index may be superior and sensitive to fluid change and more reliable in detecting decompensated heart failure.[13-15] The Medtronic Impedance Diagnostic in Heart Failure trial (MID-HeFT) study, the first of this kind, found that the OptiVol index was higher in patients with symptoms of heart failure and allowed timely intervention decreasing the cost of hospitalization.[13] Similarly, the Fluid Accumulation Status Trial (FAST) and Program to Access and Review Trending Information and Evaluate Correlation to Symptoms in Patients With Heart Failure (PARTNERS HF)[14,15] trial showed that changes in fluid index derived from intrathoracic impedance was a more accurate indicator of heart failure than daily

weight monitoring and could predict worsening heart failure in advance.[15] However, daily impedance can be affected by various factors like pleural/pericardial effusion, pneumonia (where the impedance decreases), pneumothorax (where the impedance increases), or any condition that increases intra-abdominal pressure, which will push the diaphragm up causing an increase in intrathoracic pressure and a decrease in impedance (producing a false positive reading).[16] Therefore the patient data, history, and medications should be taken in to account when utilizing OptiVol index to assist in patient management.

We present a case of pulmonary congestion due to rapid atrial fibrillation (AF) detected pre-clinically with OptiVol index.

Case Report

A 70-year-old female presented for a regular office visit. She had a Biventricular Implantable Cardioverter Defibrillator (BiV-ICD) for severe left ventricular dysfunction and left bundle branch block. She complained of non-specific fatigue for several weeks. Upon further interrogation, the fatigue coincided with some dietary indiscretion during the Christmas season. She was on a diet at that time. There was an increase in the OptiVol fluid index (see Figure 1) which was followed by atrial fibrillation (AF). The occurrence of AF led

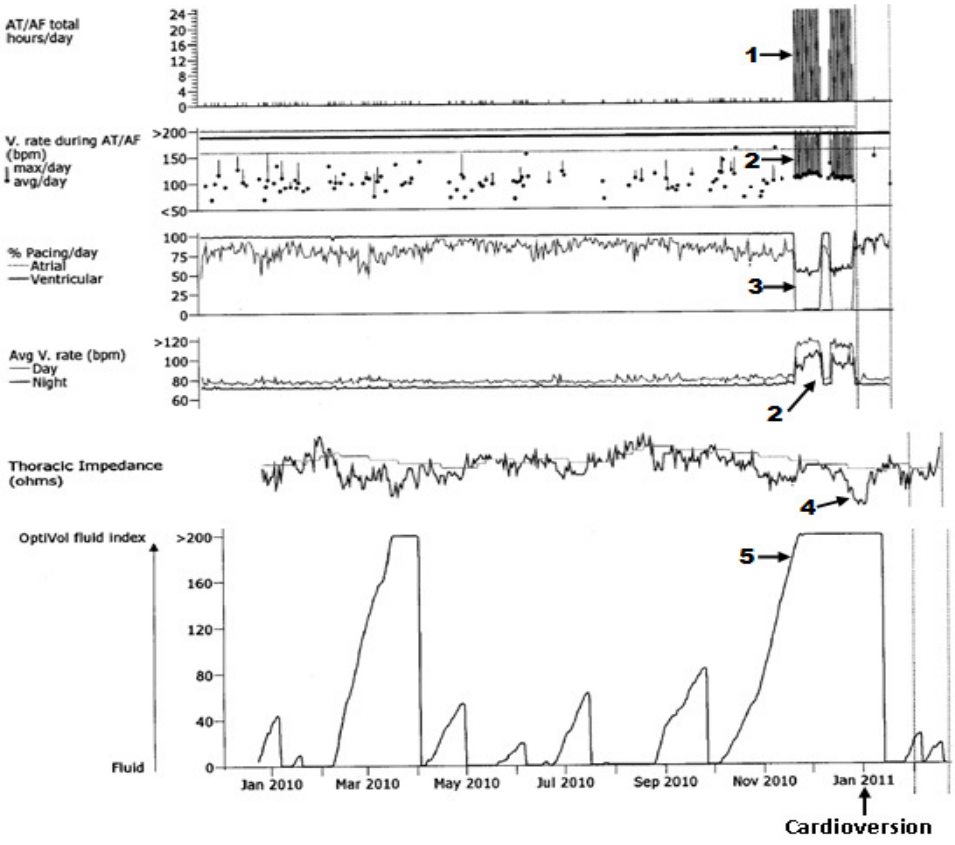

Figure 1. Initial interrogation: cardiac compass trends. 1. Atrial fibrillation. 2. High ventricular rate. 3. Diminished pacing due to atrial fibrillation. 4. Decreasing thoracic impedance. 5. Increasing fluid buildup.

to a rapid ventricular response and absent atrial pacing. The ventricular pacing also increased in duration and rate. She was cardioverted with resolution of symptoms. The OptiVol index returned to baseline.

Discussion

This case graphically demonstrated some of the cardinal pathophysiological mechanisms leading to pulmonary edema and its "preclinical" recognition by the BiV-ICD device. First, the patient indulged in a high salt meal, which increased left atrial pressure, thus precipitating atrial fibrillation. AF caused a rapid ventricular rate which increased left ventricular filling pressures and poor left ventricular filling. Ineffective atrial emptying increased back pressure towards pulmonary capillaries perpetuating the problem. Finally, she had more ventricular pacing which likely made the ventricle more dyssynchronous. All of these factors increased filling pressure on the left ventricle and left atrium giving rise to a perpetuating pulmonary edema which increased OptiVol index. Removal of rich food alone did not take care of her problem. Electrical cardioversion did.

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Keywords: heart failure, pulmonary edema, atrial fibrillation, cardiac arrhythmias, case report

Primary Small Cell Carcinoma of the Liver: A Rare and Aggressive Tumor

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Introduction

The lung is the major site for the origin of small cell carcinoma. Pulmonary small cell carcinoma of the lung comprises 20% of all lung cancers.[1-3] However, extra-pulmonary small cell carcinoma has been recognized as a separate entity.[1] Sites include the esophagus, thymus, stomach, pancreas, and the cervix. Extrapulmonary small cell carcinomas comprise only 2.5 to 4.1% of all small cell carcinomas.[1-3] Thus, primary small cell carcinoma of the liver is a rare entity. We compare the clinical course, pathology/immunohistochemical findings and treatment response among reported cases in literature.

Case Report

A 63-year-old woman presented with right upper quadrant pain of gradual onset. She denied any associated symptoms including, but not limited to, nausea, vomiting, diarrhea, fever, chills, and hematemesis. Her prior history included hepatitis C, osteoarthritis, deep vein thrombosis, and pulmonary embolism. She smoked for 20 years. Her physical exam revealed mild tenderness in the right hypochondrium and the liver edge was palpable 1 cm below right costal margin.

A complete blood count and comprehensive metabolic panel were normal. A computed tomography (CT) scan of the abdomen showed a 8.6 x 7.6 cm mass in right lobe of the liver (see Figure 1) with extension in the intrahepatic portion of the portal vein along with celiac adenopathy. Her alfa-fetoprotein was 3.48 ng/ml (0 - 6.1 ng/ml), carcinoembryonic antigen was 3.8 mg/L (0 - 5 mg/L), CA-19-9 was 86 U/ml (< 37 U/ml) and her anti-HCV was positive. Liver biopsy results were consistent with small cell carcinoma.

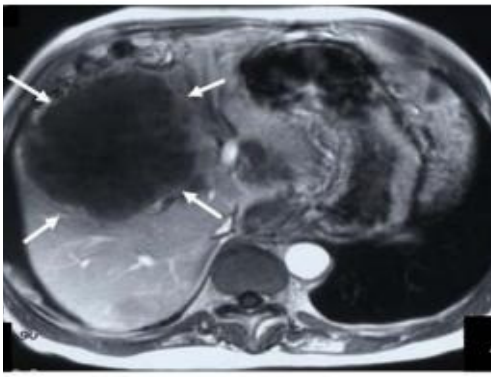

Figure 1. Arrows show a 8.6 x 7.6 cm mass in right lobe of the liver.

In search of the primary site, a chest X-ray, CT of the chest, and positron emission tomography (PET) scan were done. All were negative for any pulmonary lesion. Diagnosis of extrapulmonary small cell carcinoma of the liver was made and the patient was started on chemotherapy including carboplatin and etoposide.

Microscopically, the extrapulmonary small cell carcinoma of the liver tumor exhibited minimal cytoplasm, inconspicuous nucleoli, and diffuse nuclear hyper-chromasia. Immunohistochemical staining showed strong positivity for synaptophysin

and patchy reactivity to CK7 but was negative for AE1:3, chromogranin, CD20, CD3, HepPar1, TTF-1, CK20, and cirrhosis (Figures 2 and 3).

The patient died within 30 days of diagnosis.

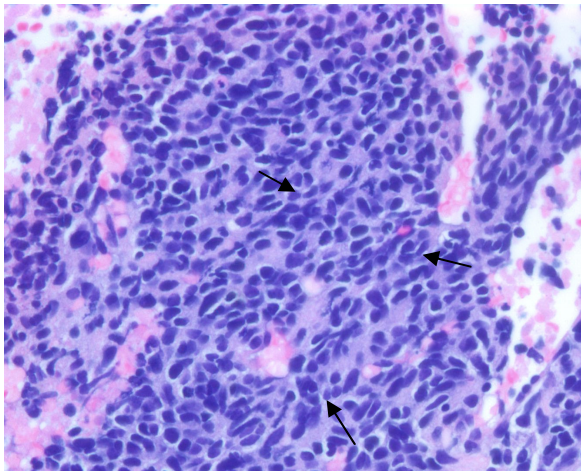

Figure 2. Tumor cells under high resolution (see arrows).

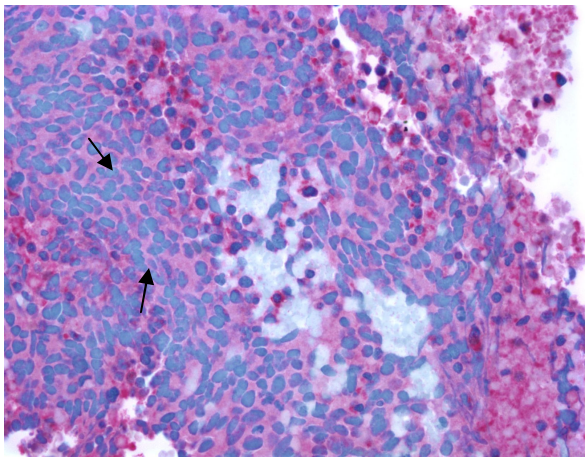

Figure 3. Arrows show positive synaptophysin stain.

Discussion

Extrapulmonary small cell carcinoma comprises 0.1 to 0.4% of all cancers.[4] Small cell carcinoma of the liver is extremely rare and only 14 cases have been reported in the literature (see Table 1). Small cell carcinoma can arise in any tissue of the body beside the lung and liver. Primary reported locations are neck, larynx, head, salivary glands, thyroid, trachea, larynx, esophagus, stomach, cervix, uterus, gall bladder, rectum, breast, and skin.[1-3] More than 50% of extrapulmonary small cell carcinomas are located in the gastrointestinal tract.[11]

Small cell carcinoma of the liver has a slight male predominance with a male to female ratio of 1.8:1; approximately 86% of patients were over 50 years at the time of presentation (Table 1). Most patients presented with upper abdominal pain, lump, loss of appetite, and jaundice. On the basis of histological appearance, it is very difficult to differentiate it from metastatic pulmonary small cell carcinoma; hence, it is mandatory to have a clear chest radiograph, CT scan of the chest, negative sputum cytology, and bronchoscopy or PET scan before making the diagnosis of primary tumor.[6]

In most reported cases, the tumor showed neuroendocrine differentiation, with markers like enolase, synaptophysin and chromogranin. Most cases also reported CD56, thyroid transcription factor-1 (TTF-1), c-kit, cytokeratin, and CEA. However, it is not necessary to find all markers in every case. Presence of vimentin, desmin, CD56, chromogranin, synaptophysin, and S-100 protein is quite specific. Synaptophysin was positive in 100% of the cases and neuron specific enolase was positive in over 85% of the cases.

Due to the small number of reported cases, conclusions about the characteristics of small cell carcinoma of the liver must not be made. Small cell carcinoma of the liver may present with weight loss, jaundice, and high AFP levels as key features.[7] Features like absence of viremia, low AFP, and cirrhosis differentiate small cell carcinoma from the most predominant tumor of liver, hepatocellular carcinoma.

Prognosis of the tumor is variable depending upon its stage and location. More than 90% of cases shown in Table 1 were diagnosed at an advanced age. Overall,

Table 1. Characteristics of patients with primary small cell carcinoma of liver.

Authors	Age / Sex	Presentation	Size (cm)	Stage at Presentation	AFP (ng/ml)	Immuno-histochemical Staining	Treatment	Outcome
Ryu et al.[5]	56 / Male	Weakness, Upper abdominal pain	8	Advanced	3.24	(+) CD56, C-kit, SYN (-) TTF-1	CT (cisplastin, etopside, irinotecan)	Unknown
Kim et al.[6]	53 / Male	Palpable mass	12	Advanced	2.94	(+) CD56, NSE, C-kit, SYN, CK, EMA (-) CK 7, 8, 19, 20, AFP, CEA, TTF-1, Vimentin, Desmin)	Segmentec-tomy and CT (cisplastin, etopside)	Unknown
Zanconati et al.[7]	56 / Male	Abdominal pain	5	Limited	> 200	(+) AE1/ AE3, CK8, 18, 19, NSE, AFP, ERY-1 (-) S-100 protein, CEA	Partial hepatectomy	Unknown
Zanconati et al.[7]	69 / Male	Diabetes, Weight loss	10	Advanced	Unknown	(+) AE1/AE3, CK8, 18, 19 (-) S-100 protein, CEA	Unknown	Died of disease
Zanconati et al.[7]	89 / Male	Jaundice	6	Advanced	150	(+) AE1/AE3, CK8, 18, 19, AFP, NSE (-) CK, CEA	Unknown	Died of disease
Kim et al.[8]	67 / Male	Abdominal pain	12	Advanced	Unknown	(+) SYN, CD56, C-kit (-) CK, CEA, AFP	CT (cisplastin, epirubicin)	Unknown

Sengoz et al.[9]	73 / Female	Unknown	Unknown	Advanced	Unknown	Unknown	Right hepatectomy	Died of disease
Sengoz et al.[9]	63 / Male	Unknown	Unknown	Unknown	Unknown	Unknown	CT (cisplastin)	Died of disease
Kim et al.[1]	Unknown	Unknown	Unknown	Advanced	Unknown	(+) CHR, SYN	Unknown	Unknown
Choi et al.[10]	82 / Female	Abdominal discomfort	6.7	Advanced	3.4	(+) CD56, NSE, SYN, CHR, TTF-1, C-kit (-) Anti-hepatocyte, AFP, Vimentin, Desmin, CK7, 19, 20, CEA, S-100 protein	CT (cisplastin, etoposide)	Unknown
Morikawa et al.[11]	77 / Male	Fatigue, weakness	10	Advanced	27	(+) AE1/AE5, CAM5.2 (-) NSE, Desmin, Vimentin, CEA	CT (cisplastin, etoposide)	Died of disease
Yang-Qing Huang et al.[12]	34 / Male	Incidental finding	Unknown	Unknown	Unknown	Unknown	Right hepatectomy, segment I excision, and TACE for recurrence	Unknown
Kaman et al.[13]	40 / Female	Pain and abdominal lump	13.5	Advanced	2.1	(+) NSE, SYN (-) TTF-1, HepPar 1, CEA	Central bisectionec-tomy and CT (cisplatin, etoposide)	Unknown

Khaw et al.[14]	51 / Male	Incidental finding	3.5	Localized	Unknown	(+) CD56, SYN, CHR	Liver transplant-ation	Died of disease
Our case	63 / Female	RUQ pain	8.6	Advanced	3.5	(+) AE1, SYN, CHR, CD20, CD3 (-) HepPar1, TTF-1, CK20	CT (carboplatin, etopside).	Died of disease

RUQ = right upper quadrant, CT = Chemotherapy, AFP = Alpha-fetoprotein, CEA = Carcinoembryonic antigen, CHR = Chromogranin, CK = Cytokeratin, EMA = Epithelial membrane antigen, NSE = Neuron specific enolase, SYN = Synaptophysin, TTF-1 = Thyroid transcription factor, TACE = transcatheter arterial chemoembolization.

limited disease has a better chance of cure than extensive disease.[11] Treatment options depend upon the tumor staging, and include surgery, chemotherapy, and radiotherapy. Standard chemotherapy includes platinum-based therapy, same as that for pulmonary small cell carcinoma of the lung. In the two cases reported by Sengoz et al.[9], one patient was given chemotherapy and other was operated for right hepatectomy. Both patients survived for more than a year. Ryu et al.[5] treated their patient with platinum-based chemotherapy. The patient responded well to therapy. Out of seven deaths, five died within three months of diagnosis. Our patient was started on platinum-based chemotherapy, but unfortunately due to the aggressive nature of the disease, she died within a month after the diagnosis.

Conclusion

Small cell carcinoma of the liver is rare and details about etiology, risk factors, and treatment options are limited. Reporting more cases will help clinicians to understand the disease aggressiveness, treatment and prognosis.

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Keywords: small cell carcinoma, liver, case report

Problematic Internet Use in Adolescents: An Overview for Primary Care Providers

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Introduction

Technology use is playing an increasingly important role in the daily lives of adolescents. As many adolescents readily incorporate the internet into their lives, it is important to be aware of the negative consequences that can stem from problematic internet use.

Problematic internet use is characterized by an excessive preoccupation with internet use and a difficulty controlling urges and behaviors related to the internet.[1] This preoccupation with or use of the internet causes significant distress or impairment in social, occupational, or other important areas of functioning.[2] Though there is no listing of problematic internet use in the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR),[3] many articles have proposed ways to identify when internet use has become a problem.

Problematic internet use in adolescents can manifest in different behaviors, including online gambling, internet-enabled sexual behavior, excessive online gaming, and excessive online socialization (i.e., emailing, messaging, social network site usage).[4,5] Heavy internet use has been correlated with poor academic performance, depression, social phobia, and attention-deficit/hyperactivity disorder.[6,7] Primary care providers are often the first to intervene when problems arise with adolescents, and awareness of problematic internet use is more important than ever.

Effects of Problematic Internet Use

Problematic internet use can impact the health of adolescents negatively. Problematic internet use in adolescents is associated with psychosomatic symptoms such as lack of physical energy, weakened immunity, and lower life satisfaction.[8] Excessive internet usage can be defined as greater than or equal to 35 hours per week.[4] High levels of electronic media use by adolescents, including internet overuse, is related to poor sleep patterns and increased daytime sleepiness, decreased level of functioning during the day, and fatigue.[9-11]

Excessive time spent on the internet increases the opportunity to be victimized through unwanted sexual solicitation, exposure to pornography, and cyberbullying. One study[12] showed that 9% of youth reported unwanted sexual solicitation, 11% of youth reported an online harassment experience (cyberbullying), and 23% of youth reported unwanted exposure to pornography. Unwanted exposure to pornography can occur inadvertently while using a search engine, opening an email, or surfing the web. Experiences with unwanted sexual solicitation include unwelcome sexual comments, requests for offline contact (e.g., telephone, in-person meeting, etc.), or other unwanted sexual experiences. Of note, solicitation may occur from other minors. Although the rate of unwanted online sexual solicitation is decreasing, online harassment, or cyberbullying, is increasing.[12]

Cyberbullying includes online threats or abusive, dishonest, and offensive material posted where the victim or others can see.[13] Given the anonymous nature and lack of face-to-face contact in online communication, online bullies may become more brazen in their bullying attempts. In

traditional forms of bullying, victims can go home and escape the threats. However, with cyberbullying, the victim may receive threatening electronic communication wherever he or she is. In addition, cyberbullying does not require the aggressor to be large in physical stature or popular in social status.

Cyberbullying can reach a much larger audience than traditional bullying,[14] can result in significant distress to victims, and should be taken seriously.[15] One study[16] of adolescents found that that 42.5% of the victims of cyberbullying felt frustrated, almost 40% felt angry, and 27% felt sad. In this study, 31.9% of respondents said cyberbullying affected them at school, while 26.5% said cyberbullying affected them at home.

Youth who experienced traditional or cyber forms of bullying, as either a bully or a victim, were more likely to attempt suicide than those who had not experienced such forms of peer aggression.[17] The perpetrators of cyberbullying also are at risk for psychological, behavioral, and social problems, such as poor emotional bonds with their caregivers, substance use, delinquent behaviors, and themselves being subject to peer victimization on and offline.[18]

The effects of problematic internet use may extend to the central nervous system. One study[19] compared adolescents who spent around 10 hours per day on the internet with controls who spent less than two hours per day on the internet. Results showed that long-term problematic internet use resulted in structural alterations in the brain in adolescents with excessive internet use. Such changes included reduced gray matter volume in regions such as the right dorsolateral prefrontal cortex, right supplementary motor areas, and left rostral anterior cingulate cortex. Impairment in these regions results in decreased cognitive control. Abnormalities were consistent with previous substance abuse studies, suggesting similar mechanisms in problematic internet use and substance use.[19]

Evaluation

Diagnostic criteria for problematic internet use do not appear in the DSM-IV-TR.[3] Various instruments have adapted DSM-IV-TR criteria for substance abuse or dependence or DSM-IV-TR criteria for pathological gambling.[20] There are at least 13 instruments designed to diagnose problematic internet use,[20] such as such as the Internet Addiction Disorder Diagnostic Criteria,[21] Young's Internet Addiction Test,[22] and the Chen Internet Addiction Scale.[23]

In general, internet use is considered problematic when it begins to interfere with daily responsibilities, grades, relationships, mood, and physical health. The primary care physician may find it useful to screen routinely for problematic internet use and may ask the following questions, as adapted from those proposed by Shaw et al.[1]:

- Do you feel overly preoccupied with accessing the internet?
- Do you feel that your internet use is excessive, inappropriate, or poorly controlled?
- Has your usage of the internet ever been overly time consuming, caused you to feel upset or guilty, or led to serious problems in your life (e.g., financial or legal problems, academic problems, or relationship loss)?

Problematic internet use may be interrelated with existing comorbidities; therefore, it is difficult to determine whether this can be classified as a separate disorder.[5] Nevertheless, recognition of the manifestations of problematic internet use remains important.

Prevention and Treatment

There are no widely-accepted evidence-based treatments for problematic internet use. As mentioned, problematic internet use

may coincide with already-present psychiatric comorbidities. In fact, problematic internet use may be predicted by the presence of depression, attention-deficit/ hyperactivity disorder, social phobia, and hostility.[6] One of the various screening tools for problematic internet use is warranted when such symptoms are present.

Social anxiety may predict problematic internet use, as socially anxious people may feel that online communication is safe and poses less risk for negative evaluation.[24] One study[25] suggested that aggression, low self-control, and narcissistic personality traits may predispose individuals to become addicted to online games. Overall, the early recognition and treatment of psychiatric symptoms, according to established treatment guidelines, is crucial in mitigating future problematic internet use.[6,26]

There is no Food and Drug Administration approved medication indicated for the treatment of problematic internet use in adolescents. Hadley et al.[27] tested escitalopram in adult patients with problematic internet use. Patients showed a significant improvement of symptoms during the 10-week, open-label escitalopram phase. After this phase, subjects were blinded and randomized to either continue on escitalopram or receive placebo. Both groups showed improvement. However, no significant difference in improvement was found between the escitalopram and placebo groups. This result suggested that the placebo effect might have played a role in improvement.

In a study of 57 males ages 13-57, bupropion SR was shown to be effective in improving problematic online game play in patients with major depressive disorder.[28] Another study of 62 children with attention-deficit hyperactivity disorder and internet game addiction showed that treatment with methylphenidate significantly reduced time spent on internet.[29]

Cognitive behavioral therapy is effective in managing problematic internet use. Young et al.[30] investigated 114 adults with problematic internet use who were treated with cognitive behavioral therapy (CBT). This study showed that most clients managed their presenting symptoms by the eighth CBT session and during the six-month follow-up had sustained these results.

Young[31] suggested the following strategies to achieve recovery from problematic internet use:

- Practicing the opposite: identifying the patient's pattern of internet use and doing neutral activities during that time.
- Setting external limits: use of external prompts such as an alarm clock to prompt client to log off.
- Setting time limits and making pre-set schedules for future use.
- Making reminder cards: negative consequence of internet use are written down on a reminder card and carried at all times.
- Set task priorities: prior to using internet, the client should write down priorities of the internet session to maintain a time-limit and avoid unplanned internet surfing.

Family involvement is equally important to achieve recovery from problematic internet use and the education of guardians along with adolescents is crucial. A family-focused approach is especially relevant to the adolescent population, as their health and well-being is dependent on family circumstances and dynamics.[32] Families can monitor internet use and assist in techniques employed to reduce problematic internet use. Numerous resources are available online for use by practitioners and families. One helpful website, www.netaddiction.org, provides information about problematic internet use, self-assessment tools, and resources for professionals and families.

In cases of cyberbullying and online sexual solicitation, adolescents should be advised to avoid responding to online harassment and to block communication from the perpetrator.[33] In addition to informing parents of online harassment, adolescents should be encouraged to contact school officials if cyberbullying takes place on campus and law enforcement officials if threats have been made. The perpetrators of cyberbullying or unwanted sexual solicitation should be reported to the website moderator. Facebook and Twitter, for example, allow inappropriate content to be flagged for review by administrators.[34,35]

Parents should be advised to maintain access to their children's online accounts and to keep computers in common areas of the house. Parents can install software on computers that blocks certain types of websites, videos, and music while reporting inappropriate online communication or access. The FBI has a printable Parent's Guide to Internet Safety that outlines risky online behaviors and ways that parents can prevent danger and intervene.[36]

Conclusion

Overall, advances in technology will continue to impact the world of adolescents. It is important to evaluate the mental, emotional, and physical impact of technology regularly. Adolescents are vulnerable to new and unique issues related to the expansion of the internet. Recognizing those at risk for problematic internet use and screening regularly is essential in adolescent healthcare. It is also important to recognize and treat co-morbid disorders that may be related to the problematic internet use. Such co-morbid disorders include, but are not limited to, depression, bipolar disorder, personality disorders, and attention-deficit hyperactivity disorder. Timely recognition of problematic internet use and appropriate intervention when the presence of problematic internet use is established can enhance the mental and physical health of adolescents in this ever-evolving world.

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Keywords: internet, adolescent, addictive behavior, bullying

HEALTH COMMUNICATION

Can Facebook Tell Us Something About Regional Health Indicators?

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A short study published in the December 2, 2011 issue of *Science* highlighted the value of social networks in promoting weight loss.[1] According to the study, participants, who were paired with "friends" with similar interests, were more likely to take part in healthy behaviors. Similar findings were suggested by a study[2] conducted with diabetic patients from rural Kansas engaged in dedicated social networks. Although social media has seen an explosive evolution over the last years, limited research has been done on its value as an indicator of community health or health outcomes. The introduction of Facebook Ads, as well as its targeting engine, provides a unique opportunity to extract data to explore possible correlations between regional Facebook use and major health indicators in which peer-to-peer interaction and support could play a significant role. Thus, the question was raised, does declared interest in health and well-being on Facebook, as well as in outdoor activities, correlate with obesity indicators at the state level?

Method

Facebook Ads were used to retrieve data regarding total number of Facebook users as well as the number of users that have a stated an interest in health and well-being (IHW), and in outdoor activities (IOA). Obesity prevalence data were retrieved from the US Center for Disease Control and Prevention.[3] Microsoft Map Point was used to map the data and IBM SPSS to perform the statistical analysis.

Results

On November 30, 2011, Facebook had over 139.5 million users in the United States. Of these, about 11.5 million users (8.19%) stated on their profile that they have an IHW and over 22 million (15.8%) stated that they have an interest in IOA. The state-level prevalence of IHW users in the Facebook population is presented in Figure 1. The minimum level recorded was 6.29% (Louisiana); the maximum level was 12.15% (Vermont), with a US mean of 8.82%. For IOA users, the average was 17.56%; minimum was 10.79% (District of Columbia), and maximum was 24.66% (Montana).

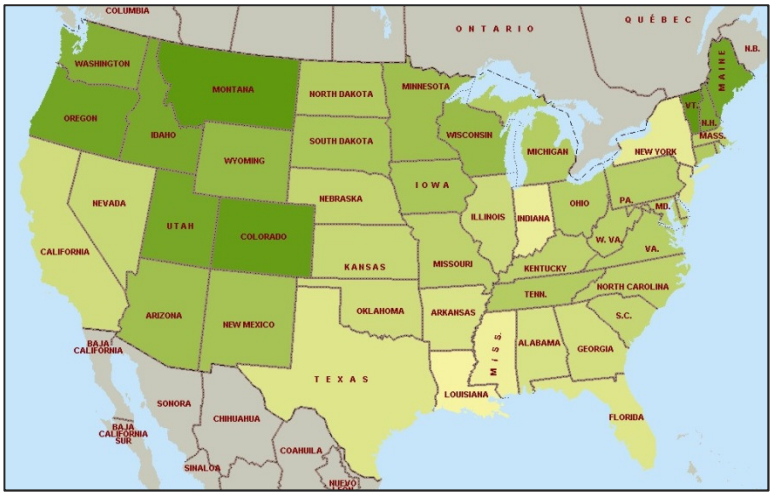

Figure 1. Percentage of Facebook users interested in Health and Well-being (green = high; yellow = low). Facebook Data, December 2011.

State-level obesity prevalence in adults 18 years and older, according to 2010 CDC data,[3] is mapped in Figure 2. The mean value for the United States was 27%; Colorado recorded the lowest level at 21%, while Mississippi recorded the highest level of obesity at 24% of the population. Percentage of IHW users was strongly correlated with obesity prevalence, $r(50) = -.460$, $p < 0.001$. No correlation was observed between percentage of IOA users and obesity rates: $r(50) = -.214$, $p > 0.05$.

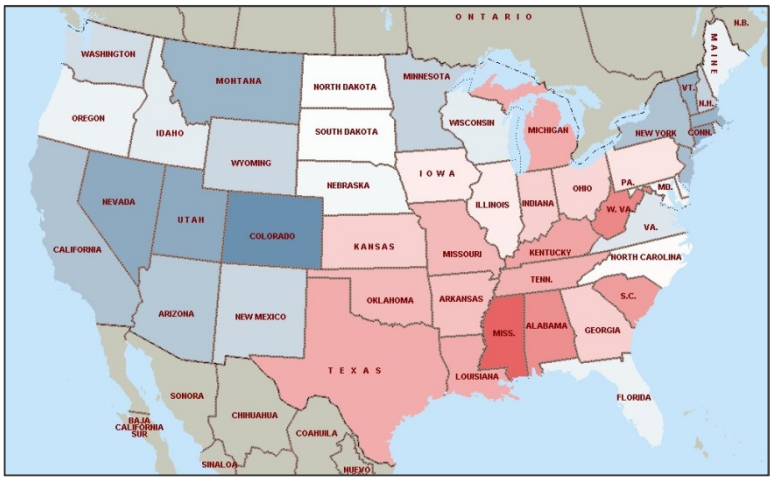

Figure 2. Obesity prevalence (red = high, blue = low).[3]

Discussion

The correlation observed in the present analysis between declared IHW users and obesity rates at state level suggested that selected Facebook demographics may have the potential to become dynamic markers of health indicators at a macrosocial level. Further studies need to address the many limitations of this anecdotal finding.

References

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