



Case Report

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Frustrations, Fascinomas and Fortuitous Findings: Medicine's Everyday Lessons in Humility

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Case Report

Fifty years after my first experience in clinical work, more than forty years after graduating from medical school, and some unexpected out-of-the clinic time due to the emergence of the SARS-CoV-2 virus, I've received the gift of some free time to pause and consider those cases that have remained ever-present in my memory, and had a profound effect on me, as a physician and person.

The summer before starting 3rd year medical school clinical clerkships, I worked in outpatient oncology clinics. Early on I came to realize that common things occurred commonly. So, "when you hear hoof beats, think of horses, not zebras". But then, a young woman came to clinic having felt a breast lump. Surprisingly, biopsy led to a diagnosis not of primary adenocarcinoma of the breast as was expected, but rather, a malignant melanoma that had metastasized from a distant primary site. This rare occurrence was called a "fascinoma" in the parlance of the senior clinic staff. And so, I was taught to "expect the unexpected", as a foundational element of critical thinking in the practice of medicine.

From these reflections, I offer a handful of cases that at the time seemed both routine, yet remarkable and memorable. Some were even worthy of publication, as referenced. While details matter a lot, for the sake of brevity I've abbreviated these cases, because mostly I want to both entertain and inspire, by sharing what is best paraphrased by a quote from Sir William Osler, "The very first step towards success in any occupation is to become interested in it." And I would humbly add, to stay interested in it.

Scared to Death

Before I began medical school I worked as a hospital orderly, the equivalent of today's medical assistant (MA). I was assigned to give daily bed baths for all the male patients in the Extended Care Unit--a lofty misnomer for an out-of-the-way and medically ignored wing of the hospital designated for those patients with incurable illnesses. When I came on duty at 7 a.m., I was assigned care of a 23-year-old man with far advanced testicular cancer who I had yet to meet. He'd been transferred to the unit late the previous day and I was told he'd been "tucked in for the night" and the last chart note recorded when he'd been admitted, stated "stable vital signs". When I entered his room, it was still dark and very quiet. I gently knocked on the door and softly announced my arrival. Receiving no response, I gently shook his shoulder. Still, no response. I turned on the room lights in full, and there he was, staring up at me but unseeing. I hadn't seen a dead person, but I knew that he was dead. He'd died alone sometime in the night. I had no idea what he experienced in his final hours or minutes of life, but I do know that in his last conscious moments, he had to be aware that he was alone. Maybe he was at peace, perhaps he was frightened or experiencing severe pain. Who's to know? It seemed to me that, among other aspects of care, he should have at least been offered companionship during what can be a terrifying time. It struck me that something needed to be done about that. Not coincidentally, the first book I wrote was entitled "The Hospice Companion" [1].

Seize the Day

I began my 3rd year of medical school clinical rotations on an



inpatient cardiology service. The first night I was on call, a lean Black man with a history of congestive heart failure and new onset ventricular ectopy was admitted. Lab testing demonstrated high digoxin levels and so the medical intern (my "boss") decided to give an intravenous loading dose of lidocaine followed by an infusion. This occurred in a setting with only continuous EKG monitoring-and me. The intern "pushed" the lidocaine, told me to "keep an eye on him", and promptly departed. Within moments the patient had a seizure and was then unresponsive. I ascertained that he had a pulse, supported his airway and established that he was breathing as I'd been taught...and yelled for help. The patient regained consciousness, and his first words were, "You're trying to kill me."

On team rounds the next morning, I described the event, having researched the pharmacology of lidocaine the prior evening when things settled down on the ward. The intern was quick to dismiss my "theory" of lidocaine toxicity, stating that it was more likely a hysterical reaction. Since I was the only witness, and "an unreliable one at that as a novice '3rd year'", his word prevailed, along with the unspoken warning, "Contradict me and pay a dear price".

Fortunately, the patient went on to recover uneventfully, with little memory of the adverse event, and later the Cardiology Fellow leading that clinical service, having interviewed and examined the patient himself shortly after the event, confided to me that he had seen lidocaine toxicity but never hysteria manifesting as was described. However, those brief moments of sheer terror, both for the patient and me, and what likely precipitated them, along with the effort at humiliation that followed, have been inexorably etched in my memory. These memories have strongly influenced my teaching, mentoring, and monitoring behaviors and interactions ever since.

I am left wondering, how many similar events, with far worse outcomes, have occurred and continue to occur due to an overtaxed system, or simply the human errors of sloppiness, lack of caring, arrogance, or other avoidable circumstances? How many others have felt as helpless as I did in a system that seemingly cannot do everything to protect vulnerable patients from harm? A clue is found in the staggering, and unchanging statistic of up to half a million iatrogenic deaths in our hospitals annually.

Imposter Syndromes

My first postgraduate year after medical school was spent at a county hospital in Northern California, serving a large indigent and immigrant community that included the Laotian "Boat People" who fled Laos due to political persecution. One night, while I was on duty in the emergency department, a lethargic, mildly jaundiced and febrile 4-year-old boy was brought in by his mother. After a thorough "work-up" to rule out infectious etiology, the only abnormal laboratory findings were anemia and a slightly elevated bilirubin level. The next day, after intravenous hydration, the boy was more energetic and afebrile. I consulted with the hospital pathologist who suggested we send a blood sample for hemoglobin electrophoresis. There was scant information about hemoglobinopathies in

the Laotian population at that time, but the case was reminiscent of thalassemia. It was determined that he had an alpha hemoglobinopathy (Hemoglobin H). Through a translator, his entire extended family (about a dozen kids and adults) was invited to provide blood samples for testing to inform them of their carrier status of this genetic variant. I left California to continue my postgraduate training in Utah shortly thereafter and lost track of this boy and his family. However, the lesson stuck with me that there are plenty of "imposters" in medicine. Because something is novel or has not been well-described in current medical literature or textbooks does not mean that it does not exist. Looking back, I regret that I didn't have the wherewithal at that time to write up a case report for publication, forewarning others to take care of these patients of this critical finding. Having now reviewed the literature from that era, it wasn't until 5 years later that someone published a similar case. Perhaps this was a lost opportunity to reduce morbidity, and even mortality, in this population.

Another "first" that came under my care that same year was a previously healthy man in his early 20's who came into the emergency department with shortness of breath and a persistent cough. He was diagnosed with pneumonia that rapidly progressed without a primary pathogen being identified. He underwent bronchoscopy that led to a diagnosis of pneumocystis carinii. It turned out that similar cases of atypical pneumonias were being reported by several San Francisco hospitals among gay men who were immunosuppressed for reasons that had yet to be well-defined. The syndrome was labelled AIDS (autoimmune deficiency syndrome) and ARC (AIDS related complex) at that time, later determined to be caused by the human immunodeficiency virus (HIV). As is now well known, that "imposter" turned out to be one of the 20th century's most vicious serial killers.

Have a Heart

Early on in my anesthesiology training, while on call at University of Utah Hospital, I was alerted to the fact we were about to proceed with the first totally artificial heart transplant on a human subject. The patient, Barney Clark, was a dentist from Seattle with end-stage heart failure. Surgery was planned for a few days later, under more controlled circumstances, but he was rapidly decompensating and the surgeon, Dr. Bill DeVries, determined that it was "go time". I was a junior on the 3-member anesthesiology team, led by Dr. Nathan Pace.

The many intra- and post-operative details of this case, both medically and ethically, are notable and much has been written about this dramatic event. What I recall the most is leaving the hospital later that next morning feeling exuberant after being part of "making medical history". That moment was short-lived because during the all-night surgery a major snowstorm had dumped more than a foot of famous Utah fresh powder on the outdoor parking lot. Somewhere underneath one of those hundreds of giant mounds of snow was my small economy-sized car. I was unprepared for this,

with neither appropriate clothing, footwear, nor any recall of where I'd parked more than 24 hours earlier--but what felt like a lifetime. Sometimes humility arrives as gently as a single snowflake; but sometimes it arrives, as then, like snowball in the face!

Too Much of a Good Thing

As a Pain Medicine Fellow at the Toronto General Hospital and The Princess Margaret Hospital (one of Canada's Regional Cancer Centers) I was often called upon to help treat oncology inpatients with a wide variety of cancer pain conditions when usual therapies were not effective at controlling pain. Opioid therapy was a commonly used modality for severe pain, and most patients did quite well when usual adverse effects, such as opioid-related constipation, were monitored and managed. An exception was a middle-aged woman with ovarian cancer who had undergone extensive pelvic surgery and was receiving an experimental regimen of post-operative chemotherapy. Her abdominal pain was very poorly controlled and only getting worse despite rapid increases in intravenously administered opioid doses. By the time I was asked to see her, she was on very high doses of hydromorphone. She was alert, tachycardic and tachypneic, with normal kidney and liver function. She was writhing in pain and could not be physically examined because even very light touch or palpation generating cries of anguish.

I had read about paradoxical responses to high dose opioids in experimental laboratory animal studies dating back decades, but as of the early 1980's, I could not find any documentation of "opioid induced hyperalgesia" in humans. Nevertheless, this patient seemed to be experiencing something akin to what had been described in those animal studies. After reducing her opioid dose by 90%, within 24 hours her pain was under control, and she was able to converse and be examined without distress. This case convinced me that the phenomenon of "opioid induced hyperalgesia" must be considered as part of the differential diagnosis of poorly controlled pain in any patient on opioid therapy.

A few years later, while serving as medical director to a community-based home hospice program, a similar case came along. This involved a woman with advanced cancer and metastatic bone disease causing excruciating pain with any type of movement. As a result, she was bedridden, on high dose opioids, and unable to interact effectively with her husband and children as she lay dying. This was neither a good way to live nor die, and by this time, I recognized the problem quickly, and initiated treatment with subcutaneously administered low-dose ketamine while concurrently reducing her opioid dose by significant increments every few hours. This provided greatly improved pain relief with mental clarity, and she was able to spend meaningful time with her family during her last few days of life. This novel approach to pain management, especially in an outpatient setting, was unusual at the time, but it has become a mainstay of palliative care in recent years [2, 3].

A Stellar Outcome

I was asked to consult on a man in his 70's with post-herpetic

neuralgia (PHN) affecting his upper chest and ipsilateral shoulder region who was hospitalized due to intractable neuropathic pain and exacerbation of COPD with respiratory failure. Attempts to treat his PHN medically with the usual analgesic and adjunctive medication had been either ineffective or caused serious adverse effects. The conundrum was that his pain restricted his breathing and that led to a vicious cycle exacerbating his COPD and right heart failure, leading to repeated hospitalizations for intubation and mechanical ventilatory support. At that time, there was consideration that PHN might be amplified, or maintained by sympathetic nervous system input, and some patients did respond to sympathetic nerve blocks.

With consent, I performed a stellate ganglion block on the affected side, leading to markedly reduced allodynia and movement-related pain, and he was able to be weaned off ventilator support and extubated. However, the results were short-lived, and repeated nerve blocks did not extend the duration of pain relief by more than a few hours. I had read that mu opioid receptors were found in sympathetic ganglia tissue, but their function had not been elucidated. Hypothesizing that these receptors might be part of sensory processing mechanisms, and with expedited Institutional Review Board compassionate use approval and fully informed consent, I set up a double-blind, controlled experiment. On alternate days, the patient would receive either local anesthetic plus low-dose fentanyl (a potent, lipophilic mu opioid agonist) via stellate ganglion block and, concurrently, intravenous saline or, local anesthetic via stellate ganglion block and fentanyl intravenously. In this way, any systemic effect of fentanyl could be readily distinguished from an effect mediated through the stellate ganglion.

As it turned out, a small amount of fentanyl added to the typical dose of local anesthetic administered as a stellate ganglion block greatly enhanced pain relief, improved function, and lasted for days rather than hours in this patient. After discharge from the hospital, he returned as an outpatient on a weekly basis for an injection. After a few weeks, the duration of pain relief became increasingly prolonged, leading to no more than monthly injections. He was never hospitalized again. Years later, he elected home hospice care for end-stage heart failure. During that last phase of his life when he wanted to stay at home, I visited him there. With full appreciation of the risks involved, and his consent, I performed local anesthetic plus low-dose opioid stellate ganglion blocks every few weeks. He remained comfortable until the time of his death from heart disease [4].

A Breakthrough

Cancer breakthrough pain is severe debilitating pain that most commonly results from a specific triggering activity in patients whose baseline cancer-related pain is well-controlled with opioid analgesics. Breakthrough pain is both prevalent and problematic for these patients. Notwithstanding the myriad issues involved in chronic opioid therapy, opioids still represent the mainstay of pain treatment in advanced cancer. At the time that oral transmucosal fentanyl citrate (OTFC) was being studied in the 1980's as a non-in-

vative means of sedating young children preoperatively for psychologically atraumatic transition to the operating room and induction of anesthesia, I was treating cancer patients with poorly controlled pain at the Salt Lake City Veterans Administration Medical Center. The pharmacokinetics of the analgesic formulations available to us at that time were not well-matched to the rapid onset and short duration of breakthrough pain episodes affecting most of these patients. Intravenous patient-controlled analgesic dosing was not then, nor now, a viable alternative for long-term episodic treatment, especially in outpatients.

Although it turned out that OTFC was not a good choice for pediatric surgical patients due to high prevalence of post-operative nausea and vomiting, it turned out to be an excellent match for opioid tolerant cancer patients, demonstrated in clinical trials initiated at that facility and then replicated over several years thereafter in multicenter studies. Over the last 25 years, the availability of approved rapid release formulations of potent opioid analgesics for cancer patients who can responsibly use and safeguard them has greatly improved cancer care. This was an example of great luck, being in the “right place at the right time” [5].

Sympathy for the Devil

The sympathetic nervous system has long been held to be a putative cause or contributor to certain types of sensory disturbances and chronic pain syndromes, such as Complex Regional Pain Syndrome. A few years into my practice a neuro-ophthalmologist referred to a patient with a highly debilitating and unusual type of eye pain. Her pain was triggered by any type of light, and it was described as “excruciating and intolerable”. This was accompanied by severe blepharospasm and uncontrolled blinking. As a result, she remained indoors with lights off and had to wear deeply tinted light-blocking glasses both indoors and outside. I had experience treating patients with somatic sensory disturbances and pain and “ruling out” a sympathetically mediated component using sympathetic nerve blocks. This patient had undergone an uncomplicated and straightforward ophthalmic surgical procedure without operative complications, post-op infection, etc., except for this residual extreme light sensitivity and reflex blepharospasm.

Similar to the patients I’d treated who had a triggering incident leading to severe pain with usually non-noxious sensory stimulation (allodynia), I wondered if light, per se, was an equivalent sensory trigger akin to gentle touch. The referring physician told me that she had several patients like this, and she was frustrated at not being able to offer them relief. We met with the patient and discussed the hypothesis that this just might be a “sympathetically maintained pain” disorder and she agreed to undergo a superior cervical sympathetic ganglion nerve block to test the hypothesis. The results were dramatic. With the onset of evidence of sympatholysis (ipsilateral Horner’s Syndrome), the patient was able to sit and converse comfortably with the lights on and without tinted glasses.

Although some psychological component of this patient’s

experience could not be ruled out, the compelling results of this procedure, in a patient who had no evident physical or emotional problems suggested that this case, and others that followed, represented an analogous complex regional pain syndrome, although with light as the sensory trigger. We attached the name “photo-oculodinia syndrome (PODS)” and introduced it, and its treatment into the literature. The importance, power, and benefit of collegial cooperation and collaboration cannot be overstated. I only wish our healthcare systems were better designed to encourage and facilitate this type of “cross-fertilization” [6].

Picture This

A woman in her 60’s with biliary cancer and severe pain, poorly responsive to usual analgesic treatment was referred to me for pain management. According to statistics, she had a poor prognosis, measured in months. She agreed to a neurolytic celiac plexus block that was facilitated using fluoroscopy to localize needle placement and deposition of neurolytic solution. She tolerated the procedure well, and her pain was well-controlled on follow-up visits. I was pleasantly surprised to see her back in clinic a year later, still thriving, but with slowly increasing abdominal pain. It was not unexpected that the nerve block was “wearing off”, likely due to nerve regeneration. This was the first time I had a patient “outlive” this type of procedure.

Within that year, real-time computed tomography (CT) had become available. This was highly fortuitous, because deposition of neurolytic solution in the right place, given anatomic changes from tumor spread and scarring from her previous injection, is challenging. The advent of this technology allowed me to visualize all vital structures and localize needle placement and injectate, avoiding tissue trauma, injury, bleeding or other morbidities, while greatly increasing the likelihood of procedural success. As it turned out, she benefited greatly, able to function through the last several months of her life at a high level without debilitating pain or adverse effects of systemic pain medications. Mostly we find humanity in the practice of medicine through the “doctor-patient” relationship---but in this case, I would have to admit that the “technology-patient relationship” was present in equal measure.

Conclusion

These clinical vignettes began with a healthcare novice’s realization that human presence is an essential component of healing, especially when cure is not possible. I concluded with an insight into the value of technology in reducing suffering in the healing arts. Clearly, both “touches” are necessary and not mutually exclusive. While curing awful diseases is every budding “Arrowsmith’s” dream, it is far more probable that throughout one’s career treating patients, it is the small “touches” we provide that will lead to immeasurable benefit to individual patients who seek care. With unfettered curiosity and a willingness to learn and make small discoveries along the way, medicine offers a lifetime of gratification unlike any other career path. It is my hope that this essay will both entertain

and inspire others to reflect on their own experiences with “frustrations, fascinomas and fortuitous findings” ---and to share them with the rest of us.

Conflict of Interest

The authors declare no conflict of interest.

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