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Pitfalls in medicine: pain out of proportion to examination findings

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Abstract

Most life-threatening conditions form a coherent clinical picture, with examination findings confirming the patient's history. However, pain out of proportion to examination findings can also signify an emergency – acute compartment syndrome, bowel ischaemia, necrotising fasciitis and acute aortic dissection may all present in this way. A lack of situational awareness leads doctors to erroneously rely on examination findings to flag impending catastrophe, but in such cases misdiagnosis or delayed treatment can have dire consequences. Patients with unexplained pain risk significant morbidity and mortality, and doctors are vulnerable to litigation and reputational damage. This article addresses this danger, exploring the causes and pathology of pain that is out of proportion, and presenting an approach to mitigate risk and prevent catastrophe.

Key words: Acute aortic dissection; Acute compartment syndrome; Acute mesenteric ischaemia; Bowel ischaemia; Necrotising fasciitis; Pain out of proportion

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Introduction

Physical examination is an essential diagnostic tool. As an adjunct to history taking, it confirms and contextualises a patient's symptoms, alluding to a diagnosis. There can be discrepancies between the patient's complaints and the doctor's findings, but in most cases, a reasonable doctor can rely on the objectivity of the examination to reveal a coherent diagnosis. However, there are times when physical examination will fail to signify impending catastrophe. Conditions such as acute compartment syndrome, bowel ischaemia, necrotising fasciitis and acute aortic dissection are time-dependent and life-threatening. They expose patients to the risk of disability and death, and expose doctors to serious medicolegal and reputational risks should they be missed. This article explores these conditions, the risks they pose, and suggests an approach to avoid this pitfall – when pain is out of proportion to examination findings.

Causes of disproportionate pain

There are many causes of pain that is out of keeping with any visible finding. The acute, life-threatening surgical conditions initially manifest subtle, if any, clinical signs. These conditions include:

- Acute compartment syndrome
- Bowel ischaemia
- Necrotising fasciitis
- Acute aortic dissection.

As time progresses, their clinical picture become clearer. By the time the diagnosis is obvious, the window for meaningful intervention may already be closed.

Many efforts have been made to empower doctors facing these situations. The literature is replete with warnings about the limitations of physical examination in the context of acute compartment syndrome. Organisations such as the World Society of Emergency Surgery have issued recommendations such as: '(s)evere abdominal pain out of proportion to physical examination findings should be assumed to be (acute mesenteric ischaemia)… until disproven' (Bala et al, 2017). A global campaign, 'Think Aorta' (https://www.thinkaorta.net), has been launched to combat misdiagnosis and treatment delays in cases of

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acute aortic dissection. One of the campaign's many achievements has been to upgrade the inter-facility transfer category of acute aortic dissection within the NHS (Heart Research UK, 2021), which will hopefully allow more rapid transfer to definitive care.

Scoring systems have been developed to aid timely diagnosis. The Laboratory Risk Indicator for Necrotising Fasciitis (LRINEC) was developed to help differentiate necrotising fasciitis from cellulitis (Wong et al, 2004). LRINEC has a high false negative rate (Neeki et al, 2017) – according to Stevens and Bryant (2017), for adults with a LRINEC score of 5.8/13 or higher, there were significant discrepancies in positive predictive values (ranging from 57% to 92%) and negative predictive values (from 86% to 96%) across several studies. This may be because 'the specificity of the LRINEC score is greatest for severe disease' (Stevens and Bryant, 2017) but, unfortunately, once severe disease is apparent, the need for a scoring system may have been obviated.

To make matters worse, the definitive management of most of the life-threatening surgical causes is invasive and the operations themselves (fasciotomy for acute compartment syndrome, laparotomy for bowel ischaemia, aggressive debridement for necrotising fasciitis) are associated with considerable morbidity (Heemskerk and Kitslaar, 2003; Tolstrup et al, 2017; Praekunatham and Tantira, 2020). This leaves clinicians with a significant dilemma: act early when the diagnosis is unclear, or act later and risk missing an opportunity. This presumes that the clinician did not overlook the diagnosis entirely.

Doctors therefore must rely on their clinical acumen, experience and specific investigations to guide their decisions, as mistaking the severity of the condition or delaying treatment poses great risks for the patient.

Risks for the patient

Acute compartment syndrome, bowel ischaemia and necrotising fasciitis can affect different areas of the body, and acute aortic dissection can affect different parts of the thoracic aorta. The complications, rates of morbidity and mortality for each of these diseases differ according to the region involved. A key determinant of the risk of complication in all cases is the time taken to institute definitive management.

In the context of acute compartment syndrome, 4 hours is a critical timeframe (Matsen, 1975), representing the threshold between reversible and irreversible muscle damage (Table 1). Acute compartment syndrome can occur in various compartments in the body. Long bone fractures account for the majority of cases, with the tibia most commonly involved (Elliott and Johnstone, 2003). Fasciotomy of the lower limb in such cases is associated with amputation rates of 11–21% and mortality rates of 11–15% (Heemskerk and Kitslaar, 2003).

Acute mesenteric ischaemia accounts for 60–70% of cases of bowel ischaemia (McKinsey and Gewertz, 1997), with a mortality rate of 60–80% (Oldenburg et al, 2004). Histopathological changes – necrosis of mucosal villi – begin just 4 hours after the onset of ischaemia (Paterno and Longo, 2008). There are several short- and long-term complications of this condition (Table 2).

Table 1. Complications of acute compartment syndrome and their relationship to the duration of ischaemia

Ischaemic duration	Complications	
30 minutes or less	Reversible neuronal damage	Paraesthesia and hyperaesthesia
2–4 hours	Reversible muscular impairment	Reversible motor weakness
>4 hours	Irreversible muscle damage	Irreversible motor weakness
	Myoglobinuria	Acute kidney injury or acute tubular necrosis
>12 hours	Irreversible neuronal damage	Volkmann's contracture or other deformity
	Myonecrosis	Gangrene
	Increased risk of infection	

From Matsen (1975)

Table 2. Complications of bowel ischaemia
Sepsis
Endotoxaemia with bacterial translocation
Bowel infarction and perforation
Gangrenous necrotic bowel
Toxic megacolon
Multi-organ failure
Fistula
Fibrosis
Colonic stricture
Short bowel syndrome (following extensive bowel resection)

From Amini and Nagalli (2021)

Table 3. Complications of necrotising fasciitis
Limb loss (Praekunatham and Tantira, 2020)
Cosmetic deformity
Sepsis (Elliott et al, 1996)
Septic shock (Elliott et al, 1996)
Renal failure (Elliott et al, 1996)
Toxic shock syndrome (Stevens, 2000)

The risk of complications in necrotising fasciitis is also time dependent (Table 3). The area of active infection can spread at 2.5 cm/hour (Sarani, 2018) and the extent of disease is an independent risk factor for mortality. The odds of mortality increase by 1.12 (90% confidence interval 1.04–1.21) for every 1% total body surface area affected (Elliott et al, 1996). A study by Praekunatham and Tantira (2020) reported an amputation rate of 8.2% and a mortality rate of 6.3%. Patients with comorbidities were at higher risk of complications, but, interestingly, diabetes mellitus was not found to be a risk factor for mortality in two studies (Elliott et al, 1996; Praekunatham and Tantira, 2020). Praekunatham and Tantira (2020) postulated that clinicians' awareness of the risk of severe infection in patients with diabetes mellitus accounts for this. Heightened awareness leading to 'early recognition and aggressive surgical treatment' caused diabetes mellitus to be a protective factor for mortality (odds ratio 0.79, 95% confidence interval 0.67–0.92), although it was a risk factor for amputation (odds ratio 6.81, 95% confidence interval 5.97–7.77).

According to Strayer et al (2012), acute aortic dissection has a mortality rate of 40% on initial clinical presentation, which increases by 1–2% every hour the patient remains untreated. From a longer-term perspective, the 1-year mortality rate in the untreated patient is 90%. The majority of cases (67%) are Stanford type A dissections affecting the proximal aorta (Evangelista et al, 2018). Outcomes are greatly improved with surgical management, the 1- and 3-year survival of surgically treated type A aortic dissection being 96.1% and 90.5% respectively (Evangelista et al, 2018). Should patients survive the acute phase, the most common complication (Table 4) is renal insufficiency (18%), followed by major brain injury (stroke and coma) (10%) and acute limb ischaemia (9.7%) (Evangelista et al, 2018).

The diagnostic difficulties deliberated

Unseen microcirculatory compromise

Three of the conditions share a pathophysiological mechanism that can cause pain: ischaemia (Figure 1). According to the arteriovenous pressure gradient theory, acute compartment

Table 4. Complications of acute aortic dissection
Stroke
Paraplegia
Acute aortic regurgitation
Myocardial infarction
Cardiac tamponade
Renal failure
Bowel ischaemia
Multi-organ failure
Acute limb ischaemia

From Matsuo (1996)

syndrome can result in an intercompartmental pressure that exceeds perfusion pressure (30 mmHg) (Elliott and Johnstone, 2003) and causes ischaemia (Whitesides et al, 1975). A reduction in pressure to the same degree in the context of intestinal ischaemia produces similar pathological sequelae (Haglund and Bergqvist, 1999). Necrotising fasciitis can result in microvascular thrombosis and vasculitis (Keller et al, 2018) which also reduces perfusion pressure, resulting in ischaemia. According to Romanelli et al (2020), '(i)schaemic pain was once thought to be a result of direct nerve injury or stimulation, but is now thought to be a symptom of the breakdown of damaged tissue and subsequent local peripheral nerve receptor activation… The sensation of ischaemic pain is of neuropathic aetiology, caused by the detection of acidosis in peripheral tissues'. It is possible that when pain is out of proportion to examination findings, it is at that time neuropathic in nature, being caused by ischaemia which is not yet clinically evident.

An obscure diagnosis

Acute aortic dissection is an exceedingly rare cause of a common presenting complaint – chest pain. While chest pain accounts for about 5% of all emergency department visits annually in the UK, only 0.0001% are cases of acute aortic dissection (Ruigómez et al, 2006; Mahase, 2020; The Health Foundation, 2020).

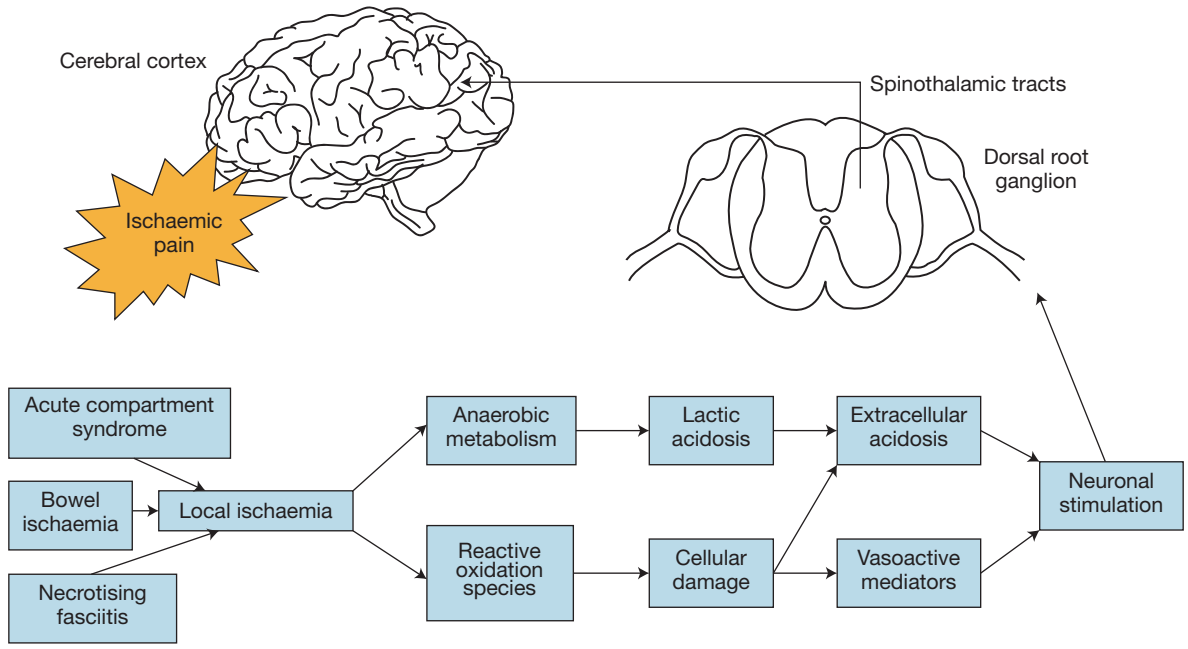

Figure 1. The pathophysiology of ischaemic pain (Das, 2015; Romanelli et al, 2020).

Around 79% of type A dissections present as typical, severe, abrupt onset chest pain (Evangelista et al, 2018), but only 25% of these patients display the other classic findings of differential blood pressures and a widened mediastinum on chest X-ray (Strayer et al, 2012). Roughly 1 in 25 patients with aortic dissection have no typical features at all. Adding to this diagnostic complexity are its plethora of possible presentations, depending on the part of the vascular tree which is affected. The obscurity of the diagnosis, therefore, lies in the dynamic nature of its pathogenesis.

Aortic dissection is a process that can also be temporally discontinuous. The patient may potentially suffer intermittent periods of severe pain, which can later affect different parts of the body or can suddenly cease.

Other conditions with few clinical features besides pain

There are many other medical and psychiatric conditions in which pain can be the predominant clinical feature (and may be out of proportion to examination findings). Examples of these include, but are not limited to, hypoadrenalism, familial Mediterranean fever, C1-esterase inhibitor deficiency, acute porphyria, complex regional pain syndrome and somatic syndrome disorders. In depth review of these is outside the scope of this article.

An approach to avoid catastrophe

Once it is established that a patient has significant pain that cannot be explained, the pain must not be dismissed (Figure 2). Efforts to communicate with the patient, senior staff and other healthcare professionals should be intensified. Empathy and concern must be communicated to the patient (Hegan, 2003). This is not only for the patient's benefit as, according to Hickson and Jenkins (2007), '…the risk (of medicolegal litigation) is predicted by the practitioner's inability to communicate effectively and establish and maintain rapport with patients, especially in the face of an adverse event'. Staff members must be made aware of the possible diagnoses. Investigations must be performed to rule out life-threatening pathology. While these are pending, the patient should undergo hourly serial examinations for at least 4 hours, preferably by the same doctor. If this is not possible, after obtaining the patient's consent, short video recordings can be used to achieve objective serial observation. If a condition becomes clinically evident while an investigation is pending, definitive surgical management must be instituted.

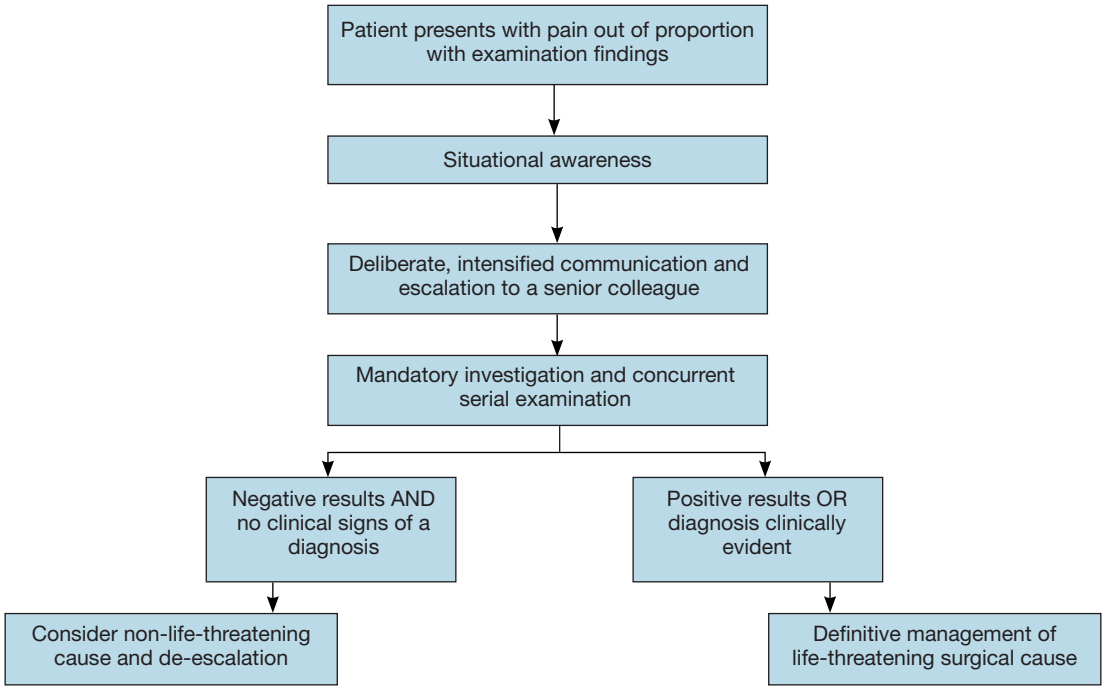

Figure 2. Risk reduction for a patient with pain out of proportion with examination findings.

Top tips

- See pain out of proportion as a red flag.
- Do not dismiss what you cannot explain or corroborate.
- Make your concerns known to everyone involved – the patient, senior colleagues and other staff members.
- Do not delay investigation or escalation to a senior.
- Examine the patient hourly while awaiting investigations or results.
- If the patient consents, use short video recordings.
- Only consider other causes of disproportionate pain once life-threatening conditions requiring surgery are ruled out.

Key points

- Pain out of proportion can indicate life-threatening pathology.
- Time is critical in avoiding catastrophic sequelae.
- Misdiagnosis and delay in treatment can lead to litigation.
- Pain out of proportion must trigger action (increased communication, monitoring and further investigation).

Conclusions

Life-threatening conditions can present with few clinical signs and disproportionate pain. Situational awareness, careful communication, intensified monitoring and mandatory investigation mitigate the risks to both patients and doctors.

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Conflicts of interest

The authors declare that there are no conflicts of interest.

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Curriculum checklist

This article addresses the following requirements from the general internal medicine curriculum:

- Communicates effectively and is able to share decision making, while maintaining appropriate situational awareness, professional behaviour and professional judgement
- Managing an acute unselected take
- Managing an acute specialty-related take
- Managing medical problems in patients in other specialties and special cases.

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