Case Report

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Refractory Response to Regional Anaesthesia: A Case of Failed Spinal and Peripheral Nerve Blocks with Negative Genetic Evaluation

Anaesthesia Section

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ABSTRACT

Failure of regional anaesthesia is often associated with technical or pharmacological errors. Only a few cases of resistance to local anaesthetics have been published in the literature, and there is no consensus on the best approach in the event of clinical suspicion. We report a case of failed regional anaesthesia in which high suspicion of resistance to local anaesthetics drugs prompted us to perform a detailed etiological investigation. We present a case of 57-year-old female who presented with difficulty in breathing, high grade fever, leg pain and swelling for two days. Patient was diagnosed with right lower leg cellulitis. Patient underwent minor dental procedure under local anaesthesia and previous caesarean section under spinal anaesthesia in past. Regional anaesthesia failed on both occasions and was converted to general anaesthesia. The patient was administered spinal anaesthesia with hyperbaric bupivacaine to undergo wound debridement but failed completely. Patient was administered combined femoral sciatic nerve block using 0.375% Ropivacaine which also failed completely. Since the patient had multiple failed regional anaesthesia attempts, we considered diagnosis of local anaesthesia resistance and proceeded with general anaesthesia. Clinical exome sequencing was conducted to identify a possible genetic basis to resistance to local anaesthetic, but no pathogenic variants were detected. This case highlights the complexity of anaesthetic resistance, the limitations of current genomic testing in explaining such phenomena, and the need for further exploration into alternative aetiology.

Keywords: Anaesthetics, Cellulitis, Drug resistance, Local, Regional

CASE REPORT

A 57-year-old female patient with BMI of 30 kg/m^2, presented to general surgeon with complaints of breathlessness, pain and swelling of the right lower limb for two days. Patient had type II diabetes mellitus for three years and was on Tablet Metformin 500 mg OD. She had a significant history of anaesthetic failure, including unsuccessful spinal anaesthesia (2ml of 0.5% hyperbaric bupivacaine) during a Lower Segment Caesarean Section (LSCS) 18 years ago, as well as ineffective regional anaesthesia (10ml of 2% lignocaine) during previous root canal treatment and minor dermatological procedures for vitiligo. No family history of resistance to local anaesthetic was reported. Local examination of right lower limb revealed warmth, tenderness, dimpled skin, blister formation and was diagnosed to have cellulitis.

Anaesthetic Management

Preoperative evaluation: On admission, patient had stable haemodynamic parameters (BP 130/80 mmHg, PR 89 beats/minute, RR 14 /minute, SPO2 99%, mMRC grading 4). CNS examination revealed no focal neurological deficit and sensory examination revealed intact pain, touch, temperature, pressure and normal motor power in all four limbs. No anatomical abnormality or infection was noted at injection site while blood investigations were within normal limits. Patient was scheduled to undergo wound debridement with fasciotomy and was assessed under ASA IIE.

Intraoperative management: Spinal anaesthesia was performed by a consultant anaesthesiologist with 10mg hyperbaric bupivacaine given after ensuring free flow of cerebrospinal fluid. We observed complete sparing of motor and sensory nerves even after waiting for 30 minutes. Since the patient had lower respiratory tract infection, we decided to avoid general anaesthesia and performed repeat subarachnoid block with 10 mg of hyperbaric bupivacaine by another consultant anaesthesiologist from local anaesthetic ampoule of the different batch. Since Spinal anaesthesia failed again, peripheral nerve block (femoral and sciatic nerve block by anterior approach) was performed under ultrasound guidance after 30 minutes, with 40 mL of 0.375% Ropivacaine, after considering local anaesthetic toxicity threshold based on patient body weight (85 kg). General anaesthesia was not contemplated due to recent respiratory infection. Despite waiting for thirty minutes, peripheral nerve block was declared a failure, necessitating conversion to Total Intravenous Anaesthesia (TIVA). Patient was induced with Inj. Propofol 120 mg and Injection fentanyl 140 mcg and airway was secured with second generation LMA (I gel) size 3. TIVA was administered by TCI pump (BD Alaris™ neXus PK Syringe Pump) with Inj. Propofol set to target plasma level of 4 µg/ml during the procedure. The patient was maintained on spontaneous ventilation with oxygen and air ratio of 2:2 throughout the procedure. Intraoperatively, haemodynamic and respiratory parameters were maintained within normal limits, 500 ml of normal saline was infused throughout the procedure while total blood loss was 80 mL. The intraoperative period was uneventful, and the patient recovered well at end of procedure. There was no residual sensory/ motor blockade of lower limb at end of surgery due to previously administerd spinal/peripheral nerve block. Patient was shifted to Post-Anaesthesia Care Unit (PACU) for observation.

Postoperative Course

The patient was monitored in the PACU for 24 hours with no significant events. Postoperative analgesia was managed with tablet Paracetamol 1g, and Inj. Tramadol 100 mg was administered for VAS >4.

Genomic Testing Findings

Targeted gene sequencing: Selective capture and sequencing of the protein coding regions and clinically relevant in the genome is performed. Variants identified in the exonic regions and splice-site are generally actionable compared to variants that occur in non-coding regions. Targeted sequencing represents a cost-effective approach to detect variants present in multiple/large genes in an individual.

Given the unusual pattern of anaesthetic insensitivity, clinical exome sequencing was performed to investigate potential genetic contributors. Sodium channel genes (e.g., SCN9A, SCN10A, SCN11A) were explicitly analysed. However, no pathogenic or likely pathogenic variants associated with anaesthetic resistance were identified. The absence of known sodium channelopathies or metabolic enzyme deficiencies suggested the involvement of yet-undiscovered mechanisms contributing to the patient's anaesthetic resistance.

This case highlights the limitations of current genetic testing in explaining anaesthetic insensitivity and emphasises the need for further research into alternative mechanisms, including epigenetic modifications and functional receptor abnormalities.

DISCUSSION

Resistance to local and regional anaesthesia is an uncommon yet challenging phenomenon that complicates perioperative management [1]. While isolated anaesthetic failures are often attributed to technical factors, systemic resistance across multiple anaesthetic techniques remains poorly understood [2-4]. Documented cases in the literature are sparse, with most reports involving insensitivity to spinal or epidural anaesthesia, and few detailing resistances across multiple regional techniques in a single patient [1,3-5].

A review of published cases reveals that anaesthetic resistance is commonly linked to sodium channel mutations (SCN9A, SCN11A), metabolic enzyme deficiencies (CYP2D6, CYP3A4), or alterations in pain processing pathways [1,6,7]. However, in this case, comprehensive genomic analysis failed to identify any pathogenic mutations, suggesting alternative mechanisms. Given the rarity of cases involving complete resistance to regional anaesthesia despite optimal technique, this report emphasises the need for further investigation into unexplored physiological or pharmacogenomic factors contributing to anaesthetic resistance.

This case is significant because it highlights the limitations of current genetic testing in explaining anaesthetic resistance and emphasises the need for further research into alternative mechanisms, including receptor dysfunction or potential epigenetic alterations. Understanding such cases is crucial for anaesthetists to develop individualised strategies for perioperative pain management in patients with a history of anaesthetic failure. This case is unique due to the patient's unexplained resistance to regional and local anaesthetic techniques, necessitating general anaesthesia for surgical management. Literature review indicates that most cases of anaesthetic insensitivity are associated with sodium channelopathies, metabolic enzyme deficiencies, or psychological factors [6,8-10]. However, in this case, genetic testing did not reveal known pathogenic variants, suggesting alternative mechanisms.

Compared to previous reports, this case is distinct due to the patient's insensitivity to local anaesthetics administered through spinal and peripheral nerve blocks [1,4]. Intraoperative details, including confirmed CSF flow and ultrasound-guided nerve block placement, rule out technical failure as a contributing factor. This highlights the need for further research into non-genetic causes of anaesthetic resistance.

Weiskopf reported failure of a spinal catheter where the position was confirmed both radiographically and with the ability to aspirate cerebrospinal fluid freely [10]. Similarly, in our case, despite the successful performance of regional anaesthetic techniques, inadequate analgesia was achieved, further substantiating the phenomenon of unexplained anaesthetic resistance.

Approach to differential diagnosis was methodical, ruling out known mutations and metabolic deficiencies. The decision to proceed with general anaesthesia was based on the complete failure of regional techniques, which aligns with similar case reports where alternative pain management strategies were required [4,11].

The perioperative anaesthetic strategy included a multimodal approach, with a backup plan for general anaesthesia, ensuring successful surgical outcomes despite resistance to regional techniques. The absence of intraoperative complications and the patient's stable postoperative course validate this approach.

Future considerations include evaluating receptor-level functional studies and refining pain management strategies for patients with suspected anaesthetic resistance. This case reinforces the importance of a structured anaesthetic approach when encountering unexplained insensitivity. This case highlights the challenges of anaesthetic resistance and the limitations of current diagnostic methods. Despite ruling out known genetic mutations, the exact cause remains unidentified, warranting further research. Negative exome sequencing does not exclude functional channelopathies or epigenetic alterations. Clinicians must adopt a systematic, individualised approach when managing patients with suspected anaesthetic resistance. A multimodal strategy, incorporating alternative techniques, is crucial when regional anaesthesia fails. Future studies should investigate non-genetic factors contributing to anaesthetic resistance to improve clinical outcomes.

CONCLUSION(S)

This case report emphasises importance of preanaesthetic evaluation for eliciting details of previous failed regional anaesthesia and plan alternate strategy to manage same. This case highlights the complexity of anaesthetic resistance, the limitations of current genomic testing in explaining such phenomena, and the need for further exploration into alternative aetiology.

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