A 15-year review of children with Kawasaki's Syndrome having general anesthesia or deep sedation

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Summary

Background: Children with Kawasaki’s syndrome (KS), also known as Kawasaki’s disease or ‘mucocutaneous lymph node syndrome’, have approximately 20–25% incidence of developing coronary artery aneurysms (CAA), stenosis or obliteration if not appropriately diagnosed and treated. In addition some children have myocarditis, pericardial effusions and/or cardiac arrhythmias during the acute phase of KS. Even with current treatment protocols, 2–4% will still be at risk of coronary artery pathology and the long-term implications regarding future coronary artery disease are unknown. Many of these children present for surgical or diagnostic procedures requiring general anesthesia or deep sedation. Only sporadic case reports have been published on the anesthetic experiences of such patients.

Methods: With Institutional Review approval, we reviewed the medical records of all children with discharge diagnosis of KS from 1985 to 2000 for those receiving general anesthesia or deep sedation. Data abstracted from the medical records included information on any surgical procedures performed any time after onset of KS symptoms, type of anesthetic, perioperative monitoring and presence or absence of operative or perioperative complications.

Results: A total of 178 children with KS were identified of whom 47 (26.4%) received either general anesthesia (34) or deep sedation (13). There were no deaths; one child developed congestive heart failure in the immediate postoperative period associated with KS myocarditis. Five (15%) of those having general anesthesia initially were either not diagnosed as having KS or had no preoperative cardiac evaluations. None of the children having general anesthesia had ST segment analysis, invasive monitoring or troponin measurements perioperatively.

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Conclusions: The high incidence of serious myocardial complications attributable to KS reported in the pediatric literature is rarely noted in the anesthesia literature. We feel there is a potential for more serious perioperative complications among KS children, although we can only speculate why complications are not more frequently encountered. Anesthetists involved in pediatric services are encouraged to consider KS in their diagnosis of children presenting with febrile illnesses with rashes and to consider the possibility of KS myocardial compromise if they encounter unexpected deterioration perioperatively. Preoperative ultrasound examination and perioperative monitoring (e.g. ST segment analysis and troponin measurements) for myocardial compromise are encouraged if KS is suspected.

Keywords: Kawasaki’s disease; anesthesia; coronary artery disease

Introduction

Kawasaki’s syndrome (KS) (1–4) has the potential for dramatic repercussions during anesthesia or deep sedation. This is attributable to the systemic vasculitis which can result in coronary artery aneurysms (CAA) (approximately 25% if untreated), and subsequent stenosis or obliteration. KS has a ubiquitous clinical presentation (Table 1) and over 4000 new cases yearly, most commonly children under 5 years of age, are hospitalized with the diagnosis in the USA (5). They can have myocarditis, arrhythmias and pericardial effusions during the acute phase while myocardial ischemia and increased mortality are noted during the first year after the acute phase as well as in older children and young adults (6–10). At present the etiology of this syndrome is still unclear but presumed to be an immune response to various stimuli (11). There is no specific laboratory test to confirm the diagnosis. It is likely that many children have had KS, but not been correctly diagnosed – often being mistaken as having nonspecific viral or common bacterial infections. The differential diagnosis may include such diverse entities as measles, toxic shock syndrome, Stevens–Johnson syndrome, and acute rheumatic fever. Children may not present with all the classic symptoms, which results in an ‘incomplete’ KS (i.e. fever for at least 5 days and presence of at least two of the clinical criteria of KS); yet they will still be at risk for CAA. Children with cardiac complications of KS can present initially in unexpected cardiac arrest (6) and the long-term cardiac ramifications are serious (7–10). In one series (7) of KS patients aged 12–39 years (mean 24.7 ± 8.4), 16% had sudden death and 61% had presented with myocardial infarction. Among those who had been correctly diagnosed and appropriately treated under current protocols – high dose aspirin (ASA) and intravenous immunoglobulin (IVIG) the incidence of complications was dramatically lowered.

We wished to review the anesthetic histories of children with KS having general anesthesia or deep sedation and identify any significant complications or untoward perioperative events.

Table 1
Diagnostic criteria for Kawasaki syndrome (2)

Fever for at least 5 days and presence of four of the five criteria below, and by the lack of another known disease process to explain the illness:
- Bilateral conjunctival injection
- Changes of the mucous membranes of the upper respiratory tract: injected pharynx; injected, fissured lips; strawberry tongue
- Polymorphous rash
- Changes of the extremities: peripheral edema, peripheral erythema, peiungual desquamation
- Cervical adenopathy

Methods

After Institutional Review Board approval, we conducted a retrospective medical record review of all
children with a discharge diagnosis of KS during a 15-year period (1985–2000) who received general anesthesia or deep sedation for a procedure either during the acute KS illness or at any time after diagnosis of KS. Each record was examined by one of the investigators and the following data abstracted: demographic data, type of procedure, anesthetic agent(s) used, time proximity from diagnosis of KS to procedure and any complications encountered.

Results
A total of 178 children with the diagnosis of KS were identified during the study period and 47 (26.4%) of those had a procedure requiring general anesthesia (n = 34) or deep sedation (n = 13). In five (15%) of the cases having general anesthesia the diagnosis of KS had not been made at the time of the anesthetic. Surgery during the acute phase of the disease included hip aspiration, exploratory laparotomy and cervical lymph node exploration; subsequent surgeries were for routine dental, orthopedic, ENT, urologic and general pediatric surgery (e.g. hernia) procedures. There were no deaths perioperatively. One undiagnosed child experienced congestive heart failure a few hours after apparently uneventful anesthesia and surgery (see case 2). There were no recognized complications during surgeries following the acute phase of the disease, but monitoring in those children did not include troponin measurement, ST segment assessment, etc.

Illustrative case reports
Case 1
This previously healthy 2-year-old male was hospitalized on illness day 3 for submandibular lymphadenitis with fever of 42.8°C that had not responded to antibiotics. He remained febrile and was noted to have bilateral nonexudative conjunctivitis and oral changes as well as laboratory parameters consistent with inflammation. The diagnosis of KS was made on illness day 5. The patient was then treated with high dose aspirin and IVIG. An echocardiogram revealed a minor pericardial effusion without evidence of coronary artery abnormalities. ECG was normal except for tachycardia. On illness day 7 he received a second dose of IVIG for persistent fever. Over the next few days he received intravenous steroids, oral cytoxan and a third dose of IVIG for ongoing signs of inflammation. A repeat echocardiogram revealed small CAA that increased in size over the subsequent 2 weeks on serial echocardiography. On day 21 he presented with abdominal pain and pallor and upon admission to hospital was noted to have ECG changes, elevated troponins and increased creatine kinase (CK-MB). At cardiac catheterization he was noted to have several coronary aneurysms (Figure 1) in the left anterior descending, circumflex and right coronary arteries. He subsequently experienced a second myocardial infarction with resulting hypokinesis of the inferior wall of the left ventricle and was anticoagulated with coumadin. One month after initial diagnosis of KS, cardiac catheterization demonstrated clot in a left coronary artery (LAD). His cardiac catheterizations were accomplished utilizing meperidine and midazolam sedation without problem.

Case 2
This previously healthy 2½-year-old child presented with 8 days of fever (39–40.6°C), erythematous rash, swollen red lips, injected conjunctivae and left hip pain with refusal to move her leg. She had received several antibiotics during her illness. Coming to the operating theater urgently in the middle of the night, 4 h after drinking milk, with a tentative clinical diagnosis of KS (by pediatricians) and septic arthritis (by orthopedic service), she had aspiration of fluid and arthroty of her hip under general anesthesia with standard, noninvasive monitoring. She had been classified ASA II-E with questionable diagnosis of KS noted in the preanesthesia record. No preoperative ECG, cardiac enzymes, chest X-ray or cardiology consultation had been obtained. She had an uneventful rapid sequence induction with thiopental, rocuronium, and isoflurane. She received approximately 20 ml·kg⁻¹ i.v. fluids and had 15 ml blood drawn under anesthesia for laboratory studies. Her intraoperative course was unremarkable. The following morning physical examination revealed grunting respirations, tachycardia, grade 1–2/6 systolic murmur and a ‘gallop’ on auscultation. SpO₂ was 82% on room air. Chest X-ray revealed cardiomegaly. Cardiology consultation confirmed a tentative diagnosis of myocarditis and...
KS. Echocardiography demonstrated ‘pipe stemming’ of the coronary arteries with dilatation and wall thickening compatible with arteritis, as well as pericardial and pleural effusions. No aneurysms were noted. She was treated with a diuretic and fluid restriction for her heart failure, and begun on high-dose ASA and IVIG (2 g·kg⁻¹) on day 9 of her illness. Cultures of the hip aspirate were sterile. Follow-up echocardiography revealed a mildly dilated coronary artery.

**Discussion**

Our case 1 example illustrates the rapid progression and progressive deterioration of children with KS even in the face of seemingly appropriate therapy. A pericardial effusion was present by illness day 5 and myocardial infarction occurred before the third week following his initial illness despite IVIG administration. Case 2 reflects the unfamiliarity of surgical services with KS, and the unfortunate position of the anesthetist providing care for a child at potentially high risk of unsuspected coronary artery disease or other cardiac impairment. This complication was unanticipated; the child seemed stable during the anesthesia and received no excess intravenous fluids perioperatively but was in florid congestive heart failure only a few hours later.

The scant anesthesia literature on KS consists primarily of single case reports. McNiece and Krishna (12) published the initial paper addressing the issues involved. Ten years later Waldron (13) described the case of a 10-year-old child with KS who developed gangrene of the foot following cardiac catheterization (attributed to his underlying vasculitis) and subsequently died 16 days later. Thomas and McEwan (14) described a 13-month-old child with Down’s and Beckwith–Weidemann syndromes, on warfarin for KS-associated coronary aneurysms, who presented to the operating theater with signs of clinical hypovolemic shock following laceration of his tongue.

We are concerned that an increasing number of children with KS (many undiagnosed) will be presenting for anesthesia and surgery and that we may be witnessing an increasing incidence of complications as a result of underlying myocarditis and arrhythmias during the acute phase, or subsequent myocardial ischemia pathology. A recent report (15) on KS from two Italian pediatric centers noted among those children initially presenting with symptoms of ‘acute abdominal pain’, nine of 10 (90%) had general anesthesia (no information provided) for surgical procedures prior to the diagnosis of KS and five (50%) subsequently developed CAA despite IVIG therapy. In this series the aneurysms
occurred between 10 and 18 days after onset of fever.

Earlier consideration of KS in the 15% of undiagnosed KS cases in our series might have deferred the decision to proceed with immediate surgery. The children possibly might have been spared an ‘unnecessary’ anesthetic (e.g. lymph node biopsy) or where the surgeons felt compelled to take the children to the operating room (e.g. possible septic hip), the anesthetist would have had a better opportunity to assess the child, minimize risk variables such as ‘full stomach’ (e.g. our case 2) and had benefit of cardiology consultation with echocardiography preoperatively. It is particularly difficult to diagnose younger children for KS, and ultrasound examination for cardiac involvement is recommended in possible cases (16).

The anesthetist must consider both the acute (e.g. myocarditis, arrhythmias and pericardial effusion) and chronic (e.g. coronary artery stenosis/obliter- ation, prior myocardial infarction) manifestations of KS. We are only now beginning to encounter older KS patients who have entered adolescence and adulthood with new challenges such as pregnancy (17). ECG monitoring for ST-segment analysis is not routinely performed at our pediatric facility periop- eratively, although the advantages of this in pediatric cases have been previously published (18) and recommended specifically in cases of KS (12, 13). Likewise none of these children having general anesthesia had perioperative serial troponin measurements (19). The reports describing anesthesia for coronary artery bypass (20, 21) and cardiac transplanta- tion surgery following KS (22) illustrate the severity of the myocardial implications of KS.

The myocardial complications (e.g. myocarditis, pericardial effusions, coronary aneurysms, infarctions, etc.) attributable to KS reported in the pediatric literature are rarely noted in the anesthesia literature. We can only speculate on why such complications are not more frequently encountered. Most anesthet- ics are performed early in the course of the disease prior to the onset of myocardial involvement or carried out at a much later date when the children are stable. Nonetheless we are concerned that five of the 47 children (15%) having general anesthesia in our series did not have a diagnosis of KS at the time of surgery nor did nine children with acute abdomen presentation as reported by Zulian et al. (15).

As illustrated by our case presentations (e.g. infarctions/myocarditis), children having KS could be at significant risk of cardiovascular compromise during anesthesia. Ideally it would be desirable to know preoperatively which children have, or previously had, KS in order to plan an appropriate anesthetic approach including choice of agents, techniques and monitoring. Anesthetists involved in pediatric services are encouraged to consider KS in their diagnoses of children presenting with fever and rashes and to consider the possibility of KS myocardial compromise if they encounter unex- pected perioperative deterioration in this group. Preoperative ultrasound examination and monitor- ing (e.g. ST segment analysis and troponin measurements) for myocardial compromise are encouraged if KS is suspected.

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