CASE REPORT

Lymph-node-first Kawasaki disease and giant coronary artery aneurysm

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SUMMARY

A 8-year-old Irish ethnicity girl presented with 3 days of fever with right-sided neck swelling which was first thought as acute tonsillitis with right-sided lymphadenitis. She was started on intravenous antibiotics. At day 7 of illness, she was diagnosed to have Kawasaki disease with clinical and biochemical evidence. Echocardiogram at day 9 of illness and subsequently CT cardiac angiogram performed revealed giant aneurysm at the right coronary artery with non-obstructing thrombus seen. The patient then commenced on clopidogrel and continued with a regular dose of aspirin. Due to the evidence of thrombus with a giant coronary aneurysm, she was also put on long-term warfarin therapy with regular monitoring of her international normalised ratio to be kept at the range of 2.0–3.0.

BACKGROUND

It is difficult to differentiate bacterial cervical lymphadenitis and lymph-node-first Kawasaki disease. Due to this fact, there might be a delay in treating lymph-node-first Kawasaki disease appropriately increasing the risk of developing coronary artery disease. This case is important as the patient was treated as right cervical lymphadenitis with multiple antibiotics as she only presented with fever and enlarged right cervical lymph nodes. However, she developed other characteristics of Kawasaki after few days leading to the diagnosis hence the appropriate treatment. As lymph-node-first Kawasaki disease is rare, paediatrician and clinician should be aware of its presence and delay of treatment may result in unfavourable cardiac problems.

This case is also important as it outlines what additional treatment a patient should have when there is a presence of giant coronary artery aneurysm with thrombus formation. The site of the giant coronary artery aneurysm was at the distal right coronary artery that is very rarely seen and this the first case reported for having such finding in Ireland.

CASE PRESENTATION

A 8-year-old Irish ethnicity girl presented with 3 days of fever with right-sided neck swelling which was first thought as acute tonsillitis with right-sided lymphadenitis. She was started on intravenous benzylpenicillin initially, but subsequently, at day 3 of antibiotics, her temperature was still spiking and looking more toxic. Thus antibiotics were changed to intravenous metrodinazole, flucloxacillin and

ceftriaxone with the concern of evolving abscess or invasive bacterial infection and blood investigations were repeated. On day 7 of illness, along with the persistent temperature spikes, she developed bilateral non-purulent conjunctivitis, generalised maculopapular rash and becoming more irritable. With all the clinical evidence supported by the biochemical investigations, she was diagnosed with Kawasaki disease.

She was born at term with no antenatal or post-natal problems. There is no family history of any congenital heart disease or any vasculitic diseases. She received all her vaccines as according to the Irish Immunisation Schedule. There is no concern about her development and schooling.

Once she was diagnosed with Kawasaki disease, she received the appropriate treatment and responded well. As per protocol, she had an echocardiogram performed by the paediatric cardiologist and CT cardiac angiogram that showed giant coronary artery aneurysm with thrombus whereby she received aspirin, clopidogrel and long-term warfarin. The right cervical lymphadenopathy regressed slowly and subsequently resolved.

INVESTIGATIONS

First set of investigations showed C reactive protein (CRP) 215.8 mg/L, white cell count (WCC) $25.4 \times 10^9/L$, neutrophils $21.54 \times 10^9/L$, haemoglobin (Hb) 123 g/L, platelet $310 \times 10^9/L$ with normal electrolytes. Ultrasound of the neck showed multiple right sided enlarged cervical lymph nodes with a conglomerate lymph node measuring 2×1.3 cm identified at the clinically palpable site of swelling, these lymph nodes had a benign lentiform shape with preservation of the fatty hila and a normal pattern of flow, all suggestive of reactive lymph nodes, small left-sided cervical lymphadenopathy also identified. (figure 1)

On day 3 of admission she deteriorated thus investigations were repeated which showed CRP decreased to 148 mg/L, WCC $11.7 \times 10^9/L$, neutrophils $8.4 \times 10^9/L$, platelet $314 \times 10^9/L$, Hb 98 g/L but her gamma glutamyl transferase (GGT) was significantly raised at 169 U/L from 41 U/L, albumin dropped from 42 g/L to 23 g/L and her potassium from 4.0 mmol/L to 2.6 mmol/L. Repeat ultrasound of the neck showed persistent right sided enlarged cervical lymph nodes.

After receiving intravenous immunoglobulin her results improved with CRP of 34.7 mg/L, WCC $14 \times 10^9/L$, neutrophils $10 \times 10^9/L$, platelet had then raised to $689 \times 10^9/L$, Hb 99 g/L, GGT dropped

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Figure 1 Ultrasound of the neck showed multiple right sided enlarged cervical lymph nodes with a conglomerate lymph node measuring 2x1.3 cm identified at the clinically palpable site of swelling, these lymph nodes had a benign lentiform shape with preservation of the fatty hila and a normal pattern of flow, all suggestive of reactive lymph nodes, small left-sided cervical lymphadenopathy also identified.

again to 81 U/L and potassium increased slowly to 3.4 mmol/L while receiving oral potassium chloride.

Once diagnosis of Kawasaki was established, an echocardiogram was done by paediatric cardiologist and CT cardiac angiogram was performed showing fusiform aneurysm arising from the right anterior descending coronary artery measuring 13 mm anteroposterior (AP) x 15 mm transverse (TR) x 23 mm craniocaudal (CC); focal non-obstructing thrombus is also evident within the aneurysm. (figures 2 and 3)

DIFFERENTIAL DIAGNOSIS

1. Viral infections:
  - Adenovirus.
  - Enterovirus.
  - Measles.
  - Epstein-Barr virus.
  - Cytomegalovirus.
2. Bacterial infections:
  - Scarlet fever.
  - Rocky mountain spotted fever.

Figure 2 CT cardiac angiogram that showed a fusiform aneurysm arising from the right anterior descending coronary artery measuring 13 mm anteroposterior x 15 mm transverse x 23 mm craniocaudal; focal non-obstructing thrombus is also evident within the aneurysm.

Figure 3 CT cardiac angiogram that showed a fusiform aneurysm arising from the right anterior descending coronary artery measuring 13 mm anteroposterior x 15 mm transverse x 23 mm craniocaudal; focal non-obstructing thrombus is also evident within the aneurysm.

- Bacterial cervical lymphadenitis.
- 3. Rheumatological disease
  - Behcet's disease.

TREATMENT

1. For the initial diagnosis of tonsillitis with right-sided lymphadenopathy, intravenous benzylpenicillin was started at a dose of 50 mg/kg six hourly. However, as she deteriorated, the antibiotics were changed to intravenous metrodinazole 7.5 mg/kg three times a day, intravenous flucloxacillin 50 mg/kg six hourly and intravenous ceftriaxone 50 mg/kg once a day.
2. During the acute diagnosis of Kawasaki disease, she received 2 gm/kg of intravenous immunoglobulin and aspirin high dose of 25 mg/kg six hourly.
3. After she was then diagnosed to have right coronary artery giant artery aneurysm, she was started on clopidogrel 2.6 mg/kg once a day and also warfarin 0.15 mg/kg once a day together with low dose aspirin of 2.6 mg/kg once a day. Warfarin is a long-term treatment given that the evidence of thrombus together with a giant aneurysm.
4. Due to the spontaneous bruises and also epistaxis, clopidogrel was discontinued and her symptoms resolved.

OUTCOME AND FOLLOW-UP

The patient is still currently on aspirin 2.6 mg/kg once a day and warfarin 0.15 mg/kg once a day and has two weekly appointments to have her international normalised ratio check to ensure that it is in the range of 2.0–3.0 international ratios. She still has a 3–4 monthly echocardiogram to see if the size of the aneurysm is increasing or decreasing. An echocardiogram was done 3 months after the first one. It showed slightly enlarging aneurysm seen at the same site measuring 14 mm AP x 22 mm TR with no thrombus. Repeated echocardiogram recently done 2 weeks ago showed a similar size of an aneurysm with the absence of thrombus too.

DISCUSSION

Kawasaki disease is now the most common cause of acquired heart disease in children in developed countries. The disease is markedly prevalence in Japan or Japanese descent but it is

pretty rare in white children with the lowest incidence of 13.7 per 100 000 children.¹

Kawasaki disease that presents initially with just fever and lymphadenopathy may be confused with bacterial or viral cervical lymphadenopathy/lymphadenitis. Children with lymph-node-first Kawasaki disease tend to be older (4-year old versus 2-year old in classical Kawasaki disease), and have more days of fever and higher C reactive protein (CRP) levels.²

It is still difficult to diagnose lymph-node-first Kawasaki disease due to the absence of specific diagnostic tests. Study done by Kanegaye *et al*, retrospectively comparing lymph-node-first presentation of Kawasaki disease with bacterial cervical adenitis and typical Kawasaki disease showed, patients with lymph-node-first Kawasaki had lower white cell count, age-adjusted haemoglobin and initial platelet count but higher erythrocyte sedimentation rate, CRP, alanine transaminases and gamma-glutamyl transpeptidase. The sonographic findings included 5–10 mm nodes resembling a ‘cluster of grapes’ in Kawasaki disease and single well-defined, centrally hypochoic masses with surrounding normal-sized nodes in bacterial cervical lymphadenitis.³

Coronary aneurysms can develop within 10 days of the febrile illness in up to 25% untreated cases and if treated the risk is <5%.⁴ The most prevalent sites of aneurysms in the order of frequency include the proximal left anterior descending artery, proximal right coronary artery, followed by the left main coronary artery, left circumflex coronary artery and finally the distal right coronary artery as seen in our patient.⁵

By diameter, the aneurysms are categorised as small (<5 mm), medium (5–8 mm) and giant (>8 mm or Z score >10). Large or giant coronary artery aneurysms do not ‘resolve’, ‘regress’ or ‘remodel’, and they rarely rupture but virtually always contain thrombi (the oldest of which may calcify) that can become occlusive.¹ The complications from giant coronary artery aneurysms include thrombosis, rupture and long-term myocardial ischaemia. A long-term study in 1215 patients with Kawasaki disease found 64 (5%) developed giant coronary artery aneurysms. Subgroup analysis revealed regression in 3 (5%), occlusion or stenosis in 30 (47%) and myocardial infarction in 15 (23%).⁶

There is a possibility the patient may need catheter intervention procedures, stenting or even bypass heart surgery. A case report was described in Australia in 2008, a 12-year-old boy had to undergo a left internal mammary artery bypass graft to the left anterior descending coronary artery after being diagnosed previously to have giant aneurysm of the coronary artery with Kawasaki disease at age 7.⁷ Patients who are diagnosed to have giant coronary artery aneurysm should have long-term follow-up involving periodic echocardiogram, exercise stress test and possibly angiography to detect any abnormalities in order to have intervention in timely manner.

The resolution of coronary artery aneurysms depends on the initial size of the aneurysm (<5 mm is more likely to resolve than >8 mm), age of the patient at the onset of disease (more likely to resolve in those <1 year age), morphology (fusiform more likely to regress than saccular aneurysm) and location of the aneurysm (distal more likely to involute as compared with the proximal).^{8,9}

For patients at increased risk of thrombosis, for example, with large or giant aneurysms (≥ 8 mm or Z score ≥ 10) and a recent history of coronary artery thrombosis, ‘triple therapy’ with aspirin, a second antiplatelet agent and anticoagulation with

warfarin or low molecular weight heparin may be considered (class IIb; level of evidence C).¹ The combination of warfarin and aspirin is known to have high cardiac-event-free survival in patients with giant coronary artery aneurysm caused by Kawasaki disease.¹⁰ Two cases described by Lee *et al* of super-giant coronary artery aneurysm which were managed successfully in the acute phase through stabilising the haemodynamic status and maintaining anticoagulation.¹¹

Learning points

- ▶ In patients having persistent cervical lymphadenopathy with persistent temperature spikes despite intravenous antibiotics, Kawasaki disease should be considered in differential diagnosis.
- ▶ Despite treatment with intravenous immunoglobulin for patients with Kawasaki disease, there is still a risk of developing coronary artery aneurysm that may even be giant coronary artery aneurysm needing long-term follow-up.
- ▶ After diagnosing a patient with giant coronary artery aneurysm, the patient should be on treatment of aspirin combined with heparin or warfarin.
- ▶ Giant coronary artery aneurysm has a high risk of cardiac events in the future, which include myocardial infarction and heart failure.

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