Kawasaki disease in infants 3 months of age and younger: a multicentre Spanish study

Kawasaki disease (KD) is a multisystem vasculitis of small and medium vessels typical of childhood. Timely treatment with intravenous immunoglobulin (IVIG) has reduced the incidence of coronary artery abnormalities (CAAs) from 25% to approximately 4%.[1] Asian studies have focused on infants under 3 months of age, but there are no published data about these patients from Western countries.[2 3]

We reviewed 621 patients under 16 years old with a diagnosis of KD between 2011 and 2016 from a multicentre study in Spain (KAWA-RACE study); 84 hospitals participated throughout the country.

We found seven children under 90 days (1.13%), with a male predominance (6 of 7). Five presented irritability, but only two fulfilled the criteria for complete KD (table 1).[1] The following were the main laboratory findings (median, IQR): highest C reactive protein (CRP) 24 mg/L (8.48–31.4), highest erythrocyte sedimentation rate 79 mm (70–105.5), maximum and minimum platelet count 900 ×10^9/L (682–1 117) and 506 ×10^9/L (449–612), minimum haemoglobin 10 g/dL (9–10.8), maximum leucocytes 21 ×10^9/L (16.45–23.37), minimum sodium 135.5 mEq/L (133–137.5), and minimum albumin 2.9 mg/dL (2.6–3.4).

In three cases, a viral infection was diagnosed and four patients presented with CAA, but no other echocardiographic findings were detected (table 1).

The median time interval since fever onset to IVIG administration was 8 days. All patients responded well to the first dose of IVIG, and only one received concomitant intravenous steroids because he was considered to be at high risk for IVIG resistance. All CAAs were transient and resolved during follow-up (table 1).

Epidemiology is different in Western countries when compared with Asian countries, where the incidence can reach up to 264.8 cases/100 000 children <5 years of age, as in Japan 2012. In USA there is also a relatively high incidence of around 25/100 000 when compared with European countries.[1] Incidence in Spain is only known in the Catalonia region and was estimated to be 8/100 000 <5 years old (2004–2014).[4]

KD in younger children is more difficult to diagnose as it presents more frequently as incomplete KD. A study from Korea with 24 patients younger than 3 months of age describes an 87.5% of incomplete KD forms, and a mean number of major diagnostic criteria of 2.8±1.4: rash was the most common (50%) and conjunctival injection was the least common (12.5%).[3] In our population non-complete KD cases represented 71.4% of the total, rash was present in 85.7%, but cervical lymphadenopathy was the least common finding (14.3%).

When we looked at laboratory tests, our case series showed less CRP increment when compared with Asian studies, 24 mg/L (median), vs 79±52 or 78.4±69 (mean), respectively, but no other relevant differences were found.[3 5] Infections were not documented in any children from the studies of Lee *et al*, Bae *et al* or Satoh *et al*.[2 3 5] In our population, 42.8% of patients presented with a confirmed infection, but were treated for KD regardless as the role of these pathogens is unclear and the consequences of not treating KD in time could be devastating.

The incidence of CAA in our series is considerably higher when compared with others, and may be due to late diagnosis: three had aneurysms (42.8% of patients), and one had dilation, according to McCrindle Z-score classification[1] (57.14% of the total had an abnormal echo). A large Korean study with 609 patients <3 months old showed an incidence of CAA of 19.9% (116 of 583), 18% dilation and 3.4% aneurysms.[2] Echocardiographic abnormalities were detected in 25% of the Bae *et al*[3] population (three cases of valve dysfunctioning without coronary involvement), and only 12.5% were CAA. All our cases with CAA recovered completely compared with the Japanese series from Satoh *et al*,[5] where 7 of 24 patients presented CAA, but in only 2 cases these alterations persisted for 1 year (8.3%).

This multicentre study let us study an uncommon condition from a large series. Despite the small number of patients, we have observed more frequent CAA, but good response to IVIG and no long-term sequelae.

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Table 1 Diagnosis, symptoms, cardiological and microbiological findings

Age (months)	Complete Kawasaki disease	Irritability	Extremity changes	Rash	Conjunctivitis	Oral changes	Cervical lymph nodes	Microbiological findings	Cardiological findings	Z-score* (SD)	Vessels (n)	Time to resolution (weeks)
3	No	No	Yes	Yes	Yes	No	No	*Enterovirus* (CSF)	CA	2.9	1	18
1.6	No	Yes	No	Yes	No	Yes	No	No	Unremarkable	–	–	–
2.6	Yes	Yes	Yes	Yes	Yes	No	Yes	No	CA	NA	1	5
2	No	No	No	Yes	Yes	Yes	No	No	Unremarkable	–	–	–
2.2	No	Yes	No	Yes	No	No	No	No	CA	3.2	2	13
2.9	Yes	Yes	Yes	Yes	Yes	Yes	No	Adenovirus (PS)	Unremarkable	–	–	–
2.3	No	Yes	No	No	Yes	Yes	No	Coryzal symptoms	CD	2–2.5	1	–

*Maximum Z-score[1 6] all measured at acute phase.
CA, coronary aneurysm; CD, coronary dilation; CSF, cerebrospinal fluid; NA, not available; PS, pharyngeal swab.

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