

Hypocalcaemia as presenting symptom of velocardiofacial syndrome

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ABSTRACT

Hypocalcaemia due to hypoparathyroidism is a rare finding in adults. The coexistence of cardiac abnormalities may be suggestive of a hereditary syndrome. We describe a case of velocardiofacial syndrome in a woman without a family history of this disorder. The hypocalcaemia was treated with calcium and vitamin D supplementation.

KEYWORDS

Genetics, hypocalcaemia, velocardiofacial syndrome

INTRODUCTION

Velocardiofacial syndrome (VCF) was first described by Shprintzen *et al.* in 1978 and is characterised by cleft palate or velopharyngeal insufficiency, cardiac abnormalities, characteristic facies and learning disabilities.¹ It is associated with 22q11.2 microdeletion. This deletion occurs in one in 4000 births. The deletion is sporadic in most cases, but an autosomal dominant form has been described. Another clinical syndrome that results from the same developmental field defect as VCF is the DiGeorge syndrome.

Diagnosis is usually established in early childhood. Affected individuals often die young, mainly due to congenital heart disease. It is less common that VCF is diagnosed in adulthood. Three cases with DiGeorge syndrome which presented with hypocalcaemia in adulthood have been reported.^{2,3} We report another patient presenting in adulthood. This case is of a woman presenting with hypocalcaemia on routine blood examination.

CASE REPORT

A 43-year-old woman presented to the outpatient clinic of Internal Medicine with complaints of diarrhoea for four

weeks, abdominal pain and fever. Her medical history revealed surgery for a ventricular septal defect and surgery for a cleft palate in early childhood, epilepsy, absent kidney, scoliosis, recurrent pelvic inflammatory disease and depressive disorder which required treatment with antidepressants. Her family history was insignificant and she had conceived no children. She had been working in an administrative function. There was no history of learning disabilities.

On examination she had a round face with hypertelorism (*figure 1*). She was of short stature. Signs of Chvostek and Trousseau were negative.

Figure 1. Face of patient described



Photo with permission from patient.

Laboratory examination revealed a white blood cell count of $24.8 \times 10^9/l$ (4.3 to 10.0), CRP 296 mg/l (0 to 10), calcium 1.14 mmol/l (2.20 to 2.65) with an ionised serum calcium level of 0.64 mmol/l (1.12 to 1.32), phosphorus 1.86 mmol/l (0.80 to 1.40) and magnesium 0.65 mmol/l (0.70 to 1.05). The intact parathyroid hormone level was 2.2 (0 to 6.0 pmol/l), 25-hydroxy vitamin D was 57 nmol/l (25 to 150) and 1,25-dihydroxy vitamin D was 80 pmol/l (48 to 161).

ECG showed a prolongation of the QT interval (corrected QT time of 505 milliseconds).

During admission she developed spontaneous movements of her arms and legs.

She was given calcium glubionate (1080 mg calcium/24 hours) intravenously and vitamin D (alfacalcidol 0.25 µg per day), after which her calcium levels returned to normal.

A CT scan of the abdomen was performed because of persistent abdominal pain and revealed a tubo-ovarian abscess, which has been removed surgically.

After discharge she continued with calcium chewing tablets (1000 mg) and vitamin D capsules (Etalpa 2 µg). On follow-up she remained normocalcaemic.

Because of the combination of hypocalcaemia, surgery for ventricular septal defect and for a cleft palate and her facial appearance, we suspected her of having VCF syndrome. Chromosomal analysis (fluorescence *in situ* hybridisation) revealed a submicroscopic deletion of the 22q11 chromosome, consistent with the velocardiofacial syndrome.

DISCUSSION

The clinical spectrum of the VCF is very variable. Originally, VCF was characterised by cleft palate, cardiac abnormalities, characteristic facies and learning disabilities.¹ Other clinical features include short stature, thymic hypoplasia, psychiatric disorders, hypocalcaemia and renal disease.⁴ Diagnosis is usually made in early childhood. Patients with VCF diagnosed in adulthood are generally family members of previously diagnosed VCF patients (e.g. parents of children with diagnosed VCF syndrome), but rarely present with hypocalcaemia.⁵

Hypocalcaemia is relatively common in children with VCF with incidence rates varying from 17 to 60%.^{4,6,7} Especially young infants have a high incidence of hypocalcaemia.

A couple of case reports have been published on patients with VCF presenting with hypocalcaemia in adulthood. Kar *et al.* describe two patients.² The first patient was a 24-year-old woman who had a generalised seizure; blood investigation revealed hypocalcaemia. She was suspected

of a genetic syndrome because of the postnatal death of her young child. The second patient was a 52-year-old woman, diagnosed with hypocalcaemia on routine blood examination. She had a history of a congenital heart condition (patent ductus arteriosus). Chromosomal analysis of both patients revealed a submicroscopic deletion in the 22q11 region.

Van den Bosch *et al.* describe a 29-year-old woman, with tetany due to hypocalcaemia.³ Her medical history included a cleft palate at birth, recurrent pulmonary infections during childhood, growth retardation, an atrial septum defect and a right descending aorta. Chromosomal analysis revealed a chromosome 22q11.2 deletion.

Frequent causes of hypocalcaemia are hereditary or acquired hypoparathyroidism, hypomagnesaemia, chronic renal failure, lacking or ineffective active vitamin D, pseudohypoparathyroidism and severe, acute hyperphosphataemia due to tumour lysis syndrome or acute renal failure.⁸ These should always be included in the differential diagnosis of hypocalcaemia.

CONCLUSION

In a patient with hypocalcaemia and a complex medical history, the velocardiofacial syndrome should be considered, as this has great implications for future family planning and genetic counselling.

REFERENCES

1. Shprintzen RJ, Goldberg RB, Lewin ML, et al. A new syndrome involving cleft palate, cardiac anomalies, typical facies, and learning disabilities: velo-cardio-facial syndrome. *Cleft Palate J.* 1978;15:56-62.
2. Kar PS, Ogoe B, Poole R, Meeking D. Di-George syndrome presenting with hypocalcaemia in adulthood: two case reports and a review. *J Clin Pathol.* 2005;58:655-7.
3. Van den Bosch MA, Wittebol S, van Dijk H, Kramer MH. Hypocalcemic tetany as an early sign of DiGeorge syndrome in an adult woman. *Am J Med.* 2002;112:161-2.
4. Ryan AK, Goodship JA, Wilson DI, et al. Spectrum of clinical features associated with interstitial chromosome 22q11 deletions: a European collaborative study. *J Med Genet.* 1997;34:798-804.
5. Stevens CA, Carey JC, Shigeoka AO. Di George anomaly and velocardiofacial syndrome. *Pediatrics.* 1990;85:526-30.
6. Motzkin B, Marion R, Goldberg R, Shprintzen R, Saenger P. Variable phenotypes in velocardiofacial syndrome with chromosomal deletion. *J Pediatr.* 1993;123:406-10.
7. Oskarsdóttir S, Persson C, Eriksson BO, Fasth A. Presenting phenotype in 100 children with the 22q11 deletion syndrome. *Eur J Pediatr.* 2005;164:146-53.
8. Potts JT. Hypocalcemia. In: Braunwald E, Fauci AS, Kasper DL, et al (eds). *Harrison's Principles of Internal Medicine.* 15th edition. New York: McGraw-Hill; 2001. p. 2220-6.