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Takayasu's arteritis: what should the dentist know?

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Summary. Takayasu's arteritis is a chronic inflammatory disease that affects large blood vessels, especially the aorta and/or its major branches. The condition presents with segmental lesions adjacent to normal, apparently unaffected, areas. The lesions include stenosis, occlusion, dilatations or aneurysm formations along the path of the affected artery. Because of the severity of the disease and the possibility of cardiovascular complications, patients with Takayasu's arteritis require medical treatment based on immunosuppressive and antihypertensive drugs, as well as regular follow up and surgical intervention in many instances. The aim of this paper was to describe the characteristics of Takayasu's arteritis, to report dental treatment carried out on an affected patient, and to discuss the main implications and care required during routine treatment for children in the dental office.

Introduction

The first published report on Takayasu's arteritis (TA) was made in 1908 by the ophthalmologist Mikito Takayasu, who reported ocular changes such as aneurysms and arteriovenous anastomoses in patients with this disease [1]. Because this author was the first to describe the condition, it was named Takayasu's disease, but there have been many synonyms such as pulseless disease, aorta arch syndrome, idiopathic aortitis, reverse coarction and others [2,3]. Despite the varied nomenclatures suggested, recognition of the name TA has been universal [3].

Epidemiological data demonstrate that TA is more common in Asian countries [3]. An incidence of approximately 150 new cases per year has been estimated in Japan [4]. Reports from occidental countries have demonstrated that the disease may be found worldwide [3]. In Brazil, for example, TA appears to be a rarely diagnosed vasculitis [2]. The disease mainly affects females, reaching a female to male ratio of up to 8 : 1 in adulthood, although in childhood the ratio is significantly lower at 2 : 1 [1,5].

The aetiology of TA remains unknown, although autoimmune mechanisms and infections such as tuberculosis are factors that have been reported to be associated with the disease. Genetic aspects also appear to contribute to the pathogenesis [2,6].

The clinical progression of TA may be divided in acute and chronic phases. The acute phase comprises signs and symptoms of a systemic inflammatory process, such as fever, weight loss, anorexia, fainting, dizziness, nocturnal sweating, myalgia, arthralgia/arthritis, exanthema, abdominal pain, vomiting and anaemia. The chronic phase is characterized by symptomatology of vascular occlusion with the appearance of hypertension and changes in peripheral pulses such as a reduction in the pulse width of one or both arm arteries, differences in symmetric palpation of pulses (arm and radial arteries) or absence of pulse on at least one side [1,7]; however, phases are not always distinct and may occur simultaneously [3].

Diagnosis of TA in childhood is difficult because the initial stage of the disease, the duration of which is variable, may be asymptomatic or may be characterized by the presence of signs and symptoms of the acute phase. The latter may lead to an erroneous diagnosis

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such as rheumatic fever, juvenile rheumatoid arthritis or systemic lupus erythematosus [3]. There is no specific test to determine the diagnosis of TA, which is usually based on clinical and angiographic data possibly complemented by computerized tomography and magnetic resonance imaging [1–3].

The main complications of TA, besides arterial hypertension, are congestive heart failure, retinopathy, cerebrovascular accident, aortic regurgitation, vascular aneurysms and myocardial infarction [2]. Even though TA is considered a severe disease, it rarely causes death [3]. Nevertheless, the outcome depends on the medical and surgical treatment and also on cardiac involvement, severity, type of arterial hypertension and distribution of the vascular lesions [1].

Cardiac involvement is common in TA because of the presence of stenosis or vascular occlusion [3]. In these cases, the disease results in an overload in the left ventricle, heart failure, arterial hypertension and coronary and myocardial alterations [1].

Multiple therapy is usually required when there is severe arterial hypertension and the patient awaiting a surgical intervention, mainly angioplasty. The drugs currently employed for control of arterial hypertension are nifedipine, beta-blockers (preferably selective), alpha-methyldopa and conversion enzyme inhibitors [1].

Skin lesions may be present in patients with TA. One of the most common cutaneous manifestations is pyoderma gangrenosum, a disease of unknown aetiology characterized by rapidly growing painful ulcers that present overhanging edges and a necrotic central area [8]. Pyoderma gangrenosum is usually associated with the chronic phase of TA [3]. Treatment of the skin lesions is based on the administration of high doses of corticosteroids together with immunosuppressive agents such as cyclosporin, thalidomide and others [9].

Currently, all treatment remains symptomatic, as the aetiology and pathogenesis of the disease are as yet unknown [2]. Corticosteroids are the most widely employed drugs for treatment of TA and are administered in high doses during the initial stage of the disease, as they suppress the inflammatory manifestations and are helpful in the reversal of arterial stenosis. Other drugs such as cyclophosphamide, methotrexate and cyclosporin have been indicated for patients not responding to corticotherapy [1].

This case report describes dental care for a boy with TA.

Case report

A 10-year-old male patient with Takayasu's arteritis, pyoderma gangrenosum and arterial hypertension was referred to the Dental Clinic by his paediatrician. Medical treatment had been initiated at 3 years old, when the patient had presented to a dermatologist with painful cutaneous lesions characteristic of pyoderma gangrenosum, which were treated with corticosteroids.

A cardiac evaluation at 5 years of age had revealed a heart murmur and possible overload in the left ventricle. The patient had subsequently demonstrated a worsening of the disease with arterial hypertension (AP), reaching up to 200×90 mmHg, reduction in palpation of peripheral pulses and differences between the measurements of AP on the upper and lower limbs. Echocardiography had shown hypertrophy of the left ventricle and coarction of the aorta, findings that were confirmed on magnetic resonance imaging. The patient had been hospitalized for cardiac catheterization and a definitive diagnosis of TA was made, with the disease affecting the descending aorta (thoracic and abdominal) with no involvement of the renal arteries.

Although the family gave a history of cardiac and respiratory problems, there had been no infection such as tuberculosis affecting any family member or the patient. At the time of referral to the dental clinic, the patient was receiving propranolol 100 mg/day, prednisone 5 mg/day and methotrexate 6 mg/m^2/day for treatment of the disease together with ranitidine 150 mg/day, folic acid 5 mg/day and calcium carbonate 500 mg/day to control the adverse effects of the other drugs. Physical examination revealed the presence of healed cutaneous scars on both legs and abdomen, but no painful symptomatology, that would have been characteristic of active pyoderma gangrenosum (Figs 1 and 2).

Intraoral clinical inspection revealed no specific findings but the presence of supra and subgingival calculus, signs of mild gingivitis and active and chronic carious lesions in some primary teeth.

Co-ordination between the child's physician and dentist was regarded as essential for dental treatment. The physician advised that procedures such as administration of local anaesthesia with vasoconstrictors could be performed without particular risk but the importance of prophylactic antibiotic therapy was highlighted and a dose of amoxicillin at a level of 50 mg/kg 1 h before treatment and continuation of the medication for 24 h after intervention was recommended.

Fig. 1. Normal skin tissue in the knee and scar of pyoderma gangrenosum in the adjacent area.

Over a series of six appointments, clinical procedures carried out under prophylactic antibiotic cover included scaling, extractions (54, 64, 75), pulpotomy (85) and composite restoration (63, 65, 85), and application of sealants (16, 26).

Local anaesthetic employed for extractions and restorations was 3% prilocaine hydrochloride with 0·03 IU felypressin (3% Citanest™ with Octapressin, Astra, São Paulo, Brazil). Care was taken to limit the volume to two ampoules, and to use a slow injection technique.

Arterial pressure and the carotid pulse were measured before each dental session. As well as fissure sealants, preventive care included oral hygiene instructions and supervised toothbrushing. Finishing and polishing of all restorations did not require prophylactic antibiotic therapy.

Discussion

Medical and dental procedures involving mucosa or other contaminated tissues usually give rise to a

Fig. 2. Scar of pyoderma gangrenosum in the abdomen.

transitory bacteraemia that is rarely maintained for more than 15 min in healthy patients [10]. However, in patients with cardiovascular alterations some bacteria such as *Streptococcus viridans*, *Streptococcus faecalis* and *Staphylococcus aureus* may be introduced into abnormal or damaged heart valves, either into the endocardium or into the endothelium close to congenital defects, and potentially leading to endocarditis or infectious endarteritis [11].

Patients presenting congenital heart defects such as aortic stenosis, as seen in TA, are considered as being at moderate risk or susceptible to the development of infectious endarteritis after some dental procedures [10,11]. Prophylactic antibiotic therapy is therefore recommended for such patients, using the protocol proposed by the AHA (American Heart Association), which comprises a single dose of amoxicillin at a level of 50 mg/kg, but not higher than 2 g, 1 h before the dental treatment [10].

In addition to the initial 2 g (50 mg/kg) dose of amoxicillin (250 mg), the patient described in this report received an additional dose of amoxicillin every 8 h during the first day. The decision to maintain blood levels of the antibiotic for a longer period was related to the severity of the disease and also to the fact that the patient was under treatment with immunosuppressive drugs (methotrexate, thalidomide) so that resistance to infection was likely to be reduced. Dajani *et al*. [10] suggested that the AHA guidelines are not recommended as a single standard, and that clinicians should follow their own clinical judgement for individual cases or in special instances such as those described in the present paper.

In relation to procedures requiring prophylactic antibiotic cover, only in the cases of finishing and

polishing of the restorations was cover not used. According to the AHA, prophylactic antibiotic therapy is required only for procedures associated with significant bleeding, Procedures such as placement of rubber dam in restorative dentistry are not included in this list [10]. Nonetheless, Needleman [12] has shown that simple placement of rubber dam for a restorative procedure or sealant application does cause some gingival bleeding. It is difficult to know whether this is significant or not.

In one investigation blood samples from 735 children aged 2–16 years who had been submitted to differing forms of dental treatment were investigated. Four procedures yielded significant bacteraemia (higher than the baseline): dental polishing (24·4%), intraligamentary injection (96·6%), rubber dam placement (29·4%) and fitting of orthodontic bands (32·1%), demonstrating that a larger variety of dental procedures may cause bacteraemia than might be appreciated [13].

Application of local anaesthesia was indicated for most dental treatment in the patient described here. Even though the child's physician did not suggest particular restriction in the use of an anaesthetic solution with vasoconstrictor, 3% prilocaine with 0·03 felypressin was selected. This choice was because the child was receiving a nonselective β-blocker (propranolol) for control of arterial hypertension. The drug has some potential to interact with vasoconstrictors of the group of sympathomimetic amines (adrenaline, noradrenaline) and induce an increase in arterial pressure and secondary reflex bradicardia if injected into a blood vessel [14,15].

It has been suggested that adrenaline may be indicated for patients receiving nonselective β-adrenergic antagonists, but the initial dose should be kept to a minimum (approximately half an ampoule of 1 : 100 000 adrenaline) and a careful injection technique is essential in order to avoid intravasculary injection. Vital signs of the patient should be monitored before and 5 min after initial administration and before anaesthetic infiltration is continued. If there is no difficulty, further ampoules may be used after a time interval of at least 5 min [15].

Conclusions

The paediatric dentist, as a health professional, should be familiar with the main systemic diseases that may affect children. Although it is a rare condition, TA affects large blood vessels such as the aorta, causing several cardiovascular alterations, and has important implications for dental care.

Prophylactic antibiotic therapy is strongly indicated for affected patients in order to avoid dissemination and establishment of bacteria on the vascular defects characteristic of this disease. As patients with TA often receive a large variety of drugs, potential interactions between these and the anaesthetics and vasoconstrictor agents employed in dentistry should be considered when providing routine care.

Résumé. L'artérite de Takayasu est une maladie inflammatoire chronique affectant les gros vaisseaux sanguins, en particulier l'aorte et/ou ses branches majeures. Des lésions segmentaires sont présentes à côté de zones apparemment saines. Les lésions incluent sténose, occlusion, dilatations ou anévrismes le long des vaisseaux atteints. En raison de la sévérité de la maladie et de la possibilité de complication cardiovasculaire, les patients porteurs d'artérite de Takayasu nécessitent un traitement médical par médicaments immuno-suppresseurs et anti-hypertension, de même qu'un suivi régulier et une intervention chirurgicale en de nombreuses circonstances. L'objectif de cet article est de décrire les caractéristiques de l'artérite de Takayasu, décrire le traitement dentaire chez un patient malade et discuter les principales implications ainsi que les soins dentaires de routine.

Zusammenfassung. Takayasu Arteritis ist eine chronisch entzündliche Erkrankung der Gefäβe, vor allem der Aorta und ihrer Hauptäste. Es zeigen sich segmentale Läsionen, angrenzend an offenbar unbeeinträchtigte Regionen. Es kommt zu Stenosen, Gefäβverschlüssen und Aneurysmen entlang der betroffenen Arterie. Aufgrund der Schwere de Erkrankung und der potentiellen cardiovaskulären Komplikationen werden die betroffenen Patienten medikamentös mit Immunsuppressiva und blutdrucksenkenden Mitteln behandelt. Eine regelmäβige Kontrolle ist erforderlich, nicht selten auch eine chirurgische Intervention. Ziel dieser Arbeit war es, auf die Besonderheiten der Takayasu Arteriitis hinzuweisen, die Zahnbehandlung ausgeführt bei vier betroffenen Patienten zu schildern und die wesentlichen Implikationen bezüglich der Routinebehandlung betroffener Kinder in der Zahnarztpraxis zu diskutieren.

Resumen. La arteritis de Takayasu es una enfermedad inflamatoria crónica que afecta a los grandes vasos

sanguíneos, especialmente la aorta y/o sus ramas principales. La alteración se presenta con lesiones segmentarias adyacentes a áreas no afectadas aparentemente normales. Las lesiones incluyen estenosis, oclusión, dilataciones o formación de aneurismas a lo largo del trayecto de la arteria afectada. Debido a la severidad de la enfermedad y a la posibilidad de complicaciones cardiovasculares, los pacientes con arteritis de Takayasu requieren tratamiento médico basado en inmunosupresores y antihipertensivos, así como un seguimiento regular e muchas ocasiones intervenciones quirúrgicas. El objetivo de este artículo fue describir las características de la arteritis de Takayasu, para informar del tratamiento dental realizado a un paciente afectado y discutir las implicaciones principales y cuidados requeridos durante el tratamiento rutinario en niños en la consulta dental.

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