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Black aortic valve and coronary arteries in liver transplantation patient: case report

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Abstract

Background Black pigmentation of the aortic valve and coronary arteries has been reported to be caused by alkaptonuria or minocycline. In patients with liver transplantation it has been described only once, after exposure to minocycline. We report a second case of such pigmentation in a liver transplantation patient, for whom none of the known causes are an adequate explanation for this pigmentation.

Case presentation Our 56-year-old male patient showed a complex history of two liver transplantations and sleeve gastrectomy, and had neither alkaptonuria nor a history of minocycline intake. He underwent an urgent coronary bypass grafting and aortic valve replacement because of an acute coronary syndrome based on three-vessel disease and progressive aortic valve stenosis. During this procedure, the aortic valve and coronary arteries had black pigmentation.

Conclusions There are causes – other than alkaptonuria and minocycline – that can induce a black pigmentation of the aortic valve and coronary arteries. In patients with a history of liver transplantation, alteration in (dys)functional liver parenchyma or administration of substances related to the procedure of liver transplantation are possible causes. Identifying these is important because they are potentially harmful as they may induce degenerative changes and functional impairment of the aortic valve and coronary arteries. Further research is needed, but proves to be difficult due to the rare nature of this condition.

Keywords Black pigmentation, Aortic valve, Liver transplantation, Alkaptonuria, Minocycline

Background

Black pigmentation of both the aortic valve and the coronary arteries is a rare condition, and is described only sporadically [1]. There are two possible causes reported.

First, alkaptonuria is a rare genetic disorder in the metabolism of the amino-acids tyrosine and phenylalanine. This enzymatic deficiency produces homogentisic acid (HGA) which accumulates in connective tissue, resulting in a blue-black pigmentation and degeneration of the affected tissue [2]. The diagnosis is based on a triad of homogentisic aciduria, ochronosis, and degenerative joint and spine arthropathy [1–3]. The cardiovascular presentation is rare, and it mainly involves the aortic valve, characterised by pigmentation and stenosis [1].

Second, minocycline is a safe antibiotic which can induce tissue pigmentation. In five cases, a minocycline-induced heart valve pigmentation has been described [4]. Pathological findings report Perls' positive granules deposited in macrophages, and free in connective tissue [4]. No functional consequences for the aortic valve have been reported [4, 5].

Here, we report a black pigmentation of the aortic valve and coronary arteries in a liver transplantation (LT) patient, which is only the second case reported in the

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literature [5]. Apart from alkaptonuria and minocycline, other explanations should be considered, especially in the context of a LT.

Case presentation

Our 56-year-old male patient had a complex history of LT's. In 2018, he had a LT for a cryptogenic cirrhosis. A severe bacterial infection of the donor organ caused prolonged admission to the intensive care and the use of several antibiotics. Only 9 months later, he underwent a second LT for cellular rejection of the first graft. Up to now, the second donor organ had a proper function. Furthermore, he had a sleeve gastrectomy during his first transplantation, and was diagnosed with a sclerotic, mildly stenotic aortic valve (maximum pressure gradient (Pmax): 19 mmHg; aortic valve area: 1,9 cm2), which was treated conservatively.

Eighteen months after the second LT, he was admitted to our emergency department with an acute coronary syndrome. The coronary angiography showed significant three-vessel disease, and on echocardiography, he had a progressively stenotic aortic valve (P_{max}: 50 mmHg, mean pressure gradient: 30 mmHg) compared with previous tests. An ad hoc heart team agreed on an urgent surgical revascularization and aortic valve replacement.

During the on-pump coronary artery bypass grafting and aortic valve replacement, the coronary arteries and the aortic valve had a dark pigmentation. The aortic valve was tricuspid, but clearly sclerotic (cf Fig. 1). The procedure itself was uncomplicated: three bypasses were performed, and a biological valve (*Edward's Perimount Magna Ease* aortic valve prosthesis (size 25 mm)) was inserted.

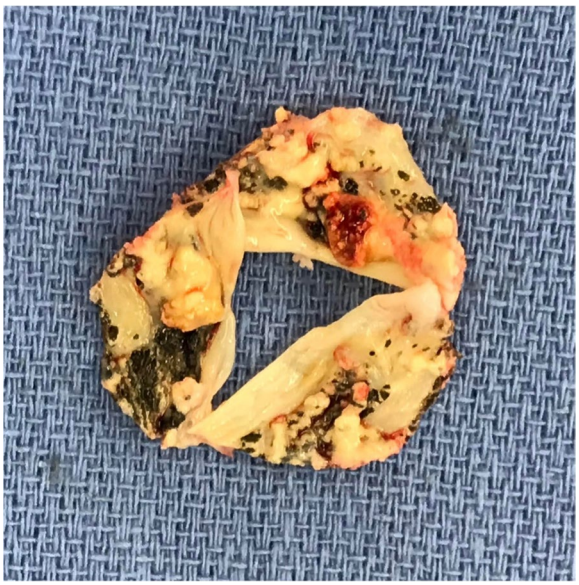

Fig. 1 Macroscopic view of the resected aortic valve leaflets with black pigmentation

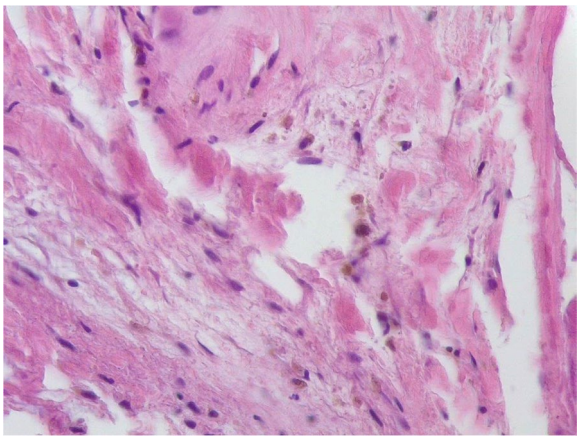

Fig. 2 Microscopic view of the pigmented valve with hematoxylin and eosin staining, detailed view of pigmented, brown-coloured macrophages

Microscopic pathological evaluation revealed valve leaflets with extensive sclerosis and calcifications. Between these calcifications and in the macrophages, there was a brown-coloured, Perls' blue positive pigment. We assumed this was suggestive for an important iron deposit accumulation (cf Figs. 2 and 3).

Postoperatively, the patient recovered well, but after a few weeks, he developed fever and pericardial fluid effusion. He was medically treated for a Dressler syndrome with a favourable outcome and no remaining complications. Patient gave his oral informed consent for his participation in the publication of this case report.

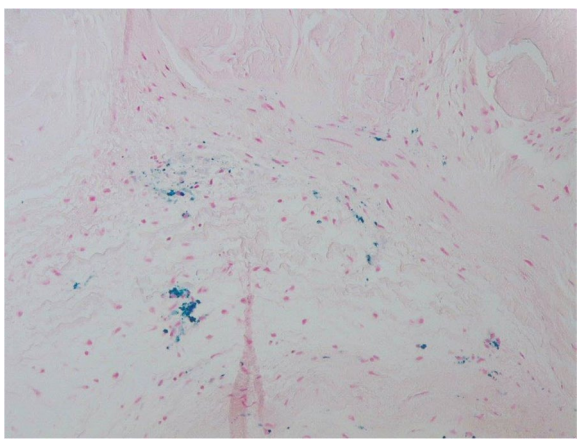

Fig. 3 Microscopic view of the pigmented valve with Perls' blue. The blue colour indicates the presence of iron deposits

Conclusions

Up to now, no liver transplantation related causes were identified as possible triggers for aortic valve pigmentation. No signs of alkaptonuria occurred, and despite the extensive use of antibiotics for the infectious complications after the first LT, no treatment with minocycline was mentioned.

Microscopic evaluation showed neither signs of alkaptonuria, nor arguments for minocycline-induced pigmentation. However, according to Tomohiro et al., the presence of Perls' blue positive granules is indicative for minocycline-induced pigmentation [4]. However, our patient was not treated with this specific antibiotic.

As a third valid possibility, we suggest a link between a complex history of LT and an unknown temporary induction of pigmentation of the aortic valve and coronary arteries. This may be caused by various medications associated with LT, or by a change in (dys)functional liver parenchyma. This latter suggestion results from a report in which LT stops further production of HGA, which in theory should cure the patient from his alkaptonuria [2]. Afterwards, neither ongoing pigmentation nor circulating HGA should be found, as was the case in our patient.

In conclusion, we suggest that, apart from minocycline and alkaptonuria, other causes of aortic valve and coronary artery pigmentation should be considered, especially in liver transplantation patients. In this specific population, the production of the causative pigment can be induced or neutralised by the change in (dys) functional liver parenchyma or can be evoked by the administration of the range of products and medications necessary for the complex procedure of liver transplantation. These causes should be considered potentially harmful, as they may induce degenerative changes and functional impairment of the aortic valve and coronary arteries. Further research is needed but is expected to be difficult because of the limited number of cases in which this condition described occurs.

Abbreviations

LT	Liver transplantation
HGA	Homogentisic acid

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Not applicable.

Authors' contributions
Patient was treated by and under supervision of HD and JR; microscopic evaluation of the valve leaflets was done by CB. SV gathered the information, did the literature review, and wrote the manuscript. The authors read and approved the final manuscript.

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Availability of data and materials
Not applicable.

Declarations

Ethics approval and consent to participate
Patient provided his oral informed consent — no written informed consent was obtained — for his participation in the publication of this case report.

Consent for publication
Patient provided his oral informed consent — no written informed consent was obtained — for his participation in the publication of this case report.

Competing interests
The authors declare that they have no competing interests.

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