Findings that shed new light on the possible pathogenesis of a disease or an adverse effect

Castleman's disease in a patient with melanoma: the role of VEGF

Lokesh Shahani

Department of Internal Medicine, Southern Illinois University School of Medicine, Springfield, Illinois, United States

Correspondence to Dr Lokesh Shahani, lokesh83@hotmail.com

Summary

Castleman's disease is a rare lymphoproliferative disorder characterised by lymph node follicular hyperplasia with abnormal interfollicular vascular growth. The authors report a female patient presenting with erythematous and pruritic skin lesion. A shave biopsy of the lesion revealed a Clark level III melanoma and sentinel lymph node biopsy revealed a microscopic focus. Staging positron emission tomography scan revealed an abnormal soft tissue mass with increased 18F-fluorodeoxyglucose accumulation in the anterior mediastinum, raising suspicions of malignancy. The patient underwent an elective resection of the mass and histological sections revealed features of Castleman's disease of the hyaline vascular type. Vascular endothelial growth factor (VEGF) has been associated with the increased vessel density in this condition. VEGF secretion by tumour cells in solid tumours such as melanomas could be a predisposing factor for Castleman's disease. Future research is needed to find an association between VEGF-secreting solid tumours and the development of lymphoproliferative tumours such as Castleman's disease.

BACKGROUND

Castleman's disease is a very rare (and thus little-known) lymphoproliferative disorder characterised by lymph node follicular hyperplasia with abnormal interfollicular vascular growth.¹ There are three histological types: hyaline vascular type showing small hyaline vascular follicles and interfollicular capillary proliferation; plasma cell type showing massive accumulation of polyclonal plasma cells in the interfollicular region; and mixed type. There is marked vascular proliferation in the interfollicular

space observed in all the variants.² We report a case of Castleman's disease which was an incidental diagnosis in a staging investigation of a patient with malignant melanoma. Vascularisation of germinal centres is a characteristic feature of Castleman's disease. Vascular endothelial growth factor (VEGF) has been associated with the increased vessel density in this condition.³ Solid tumours such as melanoma have been shown to express VEGF and VEGF has been linked to tumour angiogenesis and metastasis.⁴ VEGF secretion by tumour cells in solid tumours

Figure 1 Positron emission tomography scan showing an abnormal soft tissue mass with increased 18F-fluorodeoxyglucose accumulation in the anterior mediastinum.

such as melanomas could be a predisposing factor for Castleman's disease.

Figure 2 CT angiogram of the chest showing a hypervascular mass within the anterior mediastinum.

CASE PRESENTATION

We report a 53-year-old light eyed and fair skinned female who presented to her dermatologist with a nevus which had turned erythematous and pruritic. The patient was a non-smoker and had a pattern of social alcohol intake. Currently, she is working as a nurse and had significant sun exposure during her younger years. Her mother had a history of basal cell skin cancer which was surgically resected.

INVESTIGATIONS

A shave biopsy of the lesion revealed a Clark level III melanoma with a Breslow thickness of 0.8 mm. The lesion was reported to be focally ulcerated with two mitosis/sq. mm. The patient underwent wide excision of the melanoma. Sentinel lymph node biopsy revealed a microscopic focus of metastatic melanoma. Current National Comprehensive Cancer Network (NCCN) guidelines recommend imaging studies such as chest radiograph, CT and/or positron emission tomography (PET)-CT for confirmation of suspected metastasis or to delineate the extent of disease and may be considered to screen for recurrent/metastatic disease in patients with stage IIB-IV disease.⁵

The patient underwent a staging PET scan which revealed an abnormal soft tissue mass with increased ¹⁸F-fluorodeoxyglucose accumulation in the anterior mediastinum, raising suspicions of malignancy (figure 1). A follow-up CT angiogram of the chest delineated a hypervascular mass within the anterior mediastinum adjacent to the transverse portion of the aorta (figure 2). Due to the vascularity of the mass, it was decided to proceed with elective resection using a hemisternotomy approach. Histological sections of the mediastinal mass revealed features of Castleman's disease of the hyaline vascular type (figure 3).

Figure 3 H&E staining of the mediastinal mass—Follicle showing abnormal germinal center with marked vascular proliferation and hyalinisation.

OUTCOME AND FOLLOW-UP

The mass was completely resected. The patient was followed radiologically and had not showed any signs of recurrence of either of her malignancies.

DISCUSSION

We report a case of Castleman's disease which was an incidental diagnosis in a staging investigation of a patient with malignant melanoma. The growth of both primary and metastatic tumours is associated with the formation of new blood vessels, a process known as tumour angiogenesis.^{6 7} Angiogenesis is enhanced by several cytokines including basic fibroblastic growth factors, placental growth factors, IL-8, VEGF and others.³ VEGF is a specific mitogen for vascular endothelial cells and therefore plays a central role in angiogenesis and acceleration of microvascular hyperpermeability.⁸ In addition to its function as a proliferation factor for endothelial cells, it increases vascular permeability and may be chemotactic for monocytes.³ Vascularisation of germinal centres is a characteristic feature of Castleman's disease. VEGF has been associated with the increased vessel density in this condition.³

Solid tumours such as melanoma have been shown to express VEGF and VEGF has been linked to tumour angiogenesis and metastasis.⁴ VEGF secretion by tumour cells in solid tumours such as melanomas could be a predisposing factor for Castleman's disease. A VEGF level in our patient was not tested due to financial constraints as well as lack of current data regarding therapeutic benefit. Future research is needed to find an association between VEGF-secreting solid tumours and the development of lymphoproliferative tumours such as Castleman's disease. The confirmation of the role of VEGF in the pathogenesis of Castleman's disease may lead trial of new therapies such as anti-VEGF monoclonal antibodies or antisense oligonucleotides against VEGF mRNA for Castleman's disease.⁸

Learning points

- ▶ Castleman's disease is a rare lymphoproliferative disorder characterised by lymph node follicular hyperplasia with abnormal interfollicular vascular growth.
- ▶ Vascularisation of germinal centers is a characteristic feature of Castleman's disease. VEGF has been associated with the increased vessel density in this condition.
- ▶ Solid tumours such as melanoma have been shown to express VEGF and VEGF has been linked to tumour angiogenesis and metastasis. VEGF secretion by tumour cells in solid tumours such as melanomas could be a predisposing factor for Castleman's disease.

Competing interests None.

Patient consent Obtained.

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