Leser-Trélat Sign in Glioblastoma Multiforme

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Most patients with Leser-Trélat sign have an adenocarcinoma of the gastrointestinal tract and various types of malignancies have been reported. However, Leser-Trélat sign, in association with a brain tumor is very rare. We describe a 59-year-old Korean male, previously diagnosed with glioblastoma multiforme, who presented with eruptive seborrheic keratoses on the trunk. A comparison study of magnetic resonance images (MRI) of the brain before and after the appearance of the seborrheic keratoses showed enlargement of tumor size after the onset. After 2 additional cycles of chemotherapy, the skin lesions disappeared spontaneously and MRI showed a decrease in the tumor size.

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INTRODUCTION

Leser-Trélat sign is an increase in both the size and number of itchy, multiple, seborrheic keratoses over a short period of time, in association with internal malignancy. This change has been explained by the capacity of the internal malignancy for growth factor secretion. Although most patients with Leser-Trélat sign have adenocarcinoma of the gastrointestinal tract, there have been reported cases of Leser-Trélat sign in association with various types of malignancies including osteogenic sarcoma and Sezary syndrome. However, Leser-Trélat sign in association with a brain tumor is very rare. To our knowledge, three cases, namely primary lymphoma of the brain, germinoma, and anaplastic ependymoma, have been reported. We describe a Korean male patient with glioblastoma multiforme (GM) who developed Leser-Trélat sign, in association with disease progression.

CASE REPORT

A 59-year-old Korean man presented with a 5-month history of eruptive, pruritic, brownish skin lesions on the trunk, particularly on the lower abdomen and back. The lesions had been aggravated in the 10 day period leading up to the clinic visit. The patient had previously been diagnosed with biopsy-proven GM which had been surgically removed 2 years ago. Thereafter, he had received radiotherapy and 8 cycles of temozolomide chemotherapy. On physical examination, 2-3 mm sized, light-brownish and slightly verrucous papules were observed on the trunk, particularly on the lower abdomen and back (Fig. 1A). Histopathological examination of a skin lesion biopsied from the lower abdomen showed hyperkeratosis, parakeratosis, acanthosis, and several cystic inclusions of horny material. These findings were compatible with the acanthotic type of seborrheic keratosis. Investigations into other underlying malignancies via a chest X-ray and esophagagogastroscopeopy, did not show any remarkable findings. Magnetic resonance images
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Fig. 1. (A) Multiple 2-4 mm sized brown-colored papules on the anterior chest wall and lower abdomen (Inset: magnified view of the skin lesions). (B) Spontaneous resolution of the skin lesions.

Fig. 2. MRI of the brain show enlargement of the tumor size; (A) before and (B) after the emergence of the Leser-Trélat sign. (C) Slightly decreased tumor size 4 months after the 2 additional temozolomide chemotherapy treatments.

(MRI) of the brain showed enlargement of the tumor size compared to previous images which had been taken 6 months ago: from $39.9 \times 35.8$ mm (Fig. 2A) to $41.3 \times 39.5$ mm (Fig. 2B). Four months after a subsequent 2 additional cycles of temozolomide chemotherapy, the skin lesions disappeared spontaneously (Fig. 1B). MRI of the brain was conducted which showed a decrease of the tumor size to $38.7 \times 39.1$ mm (Fig. 2C).

DISCUSSION

Leser-Trélat sign has been defined as the eruptive appearance of seborrheic keratoses which increase in size and number over a short period of time, in association with an underlying malignancy\textsuperscript{1,2}. In addition to seborrheic keratosis, other epidermal changes including acquired ichthyosis, Cowden’s disease, acrokeratosis paraneoplastica, hypertrichosis lanuginosa and florid cutaneous papillomatosis can accompany Leser-Trélat sign\textsuperscript{1}. Because the incidence of seborrheic keratosis is high in adults, whether the coexistence is coincidental or not is still a matter of debate and the presence of the Leser-Trélat sign is not accepted by some authors. However, the eruptive nature and concomitant change in the accompanied tumor in our case report strongly indicates the validity of this disease entity. To date, there have been three reports of Leser-Trélat sign in patients with intracranial tumors, but only one case is associated with a neuroepithelial tumor\textsuperscript{2,4}. Glioma is the most common primary intracranial tumor and the World Health Organization grade IV.
glioma, or glioblastoma, is the most common malignant glioma. The cause of Leser-Trélat sign is not elucidated. Hormonal influence, particularly growth factors secreted by tumors, was suggested and Ellis et al. reported a case of malignant melanoma and Leser-Trélat sign associated with increased urinary levels of transforming growth factor-α secreted by melanoma. Dense staining for epidermal growth factor receptors in all layers of the epidermis, except for the stratum corneum, was exhibited. Five months after surgical excision of the melanoma, Ellis et al. observed a decrease in the number of seborrheic keratoses which was thought to be due to the absence of growth factor secretion. Previous reports that both glioblastoma tumor cells and proliferating endothelial cells produce connective tissue growth factor and over-express wild-type or mutant epidermal growth factor receptors provide the possible explanation for this phenomenon. Although further studies on the growth factors and growth factor receptors could not be performed in this case, the fact that a comparison study by MRI of the brain showed enlargement of the tumor size after the Leser-Trélat sign became evident, then the seborrheic keratoses spontaneously disappeared after 2 additional treatments with temozolomide chemotherapy accompanied by a decrease in the tumor size, strongly suggests that GM could have played a role in the course of the Leser-Trélat sign.

As a conclusion, in patients with rapidly developing seborrheic keratoses, it is important to investigate for underlying malignancies, and a brain tumor should be considered as one of the associated malignancies with Leser-Trélat sign.

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REFERENCES