Immunotherapy delays disease progression of high-grade meningiomas

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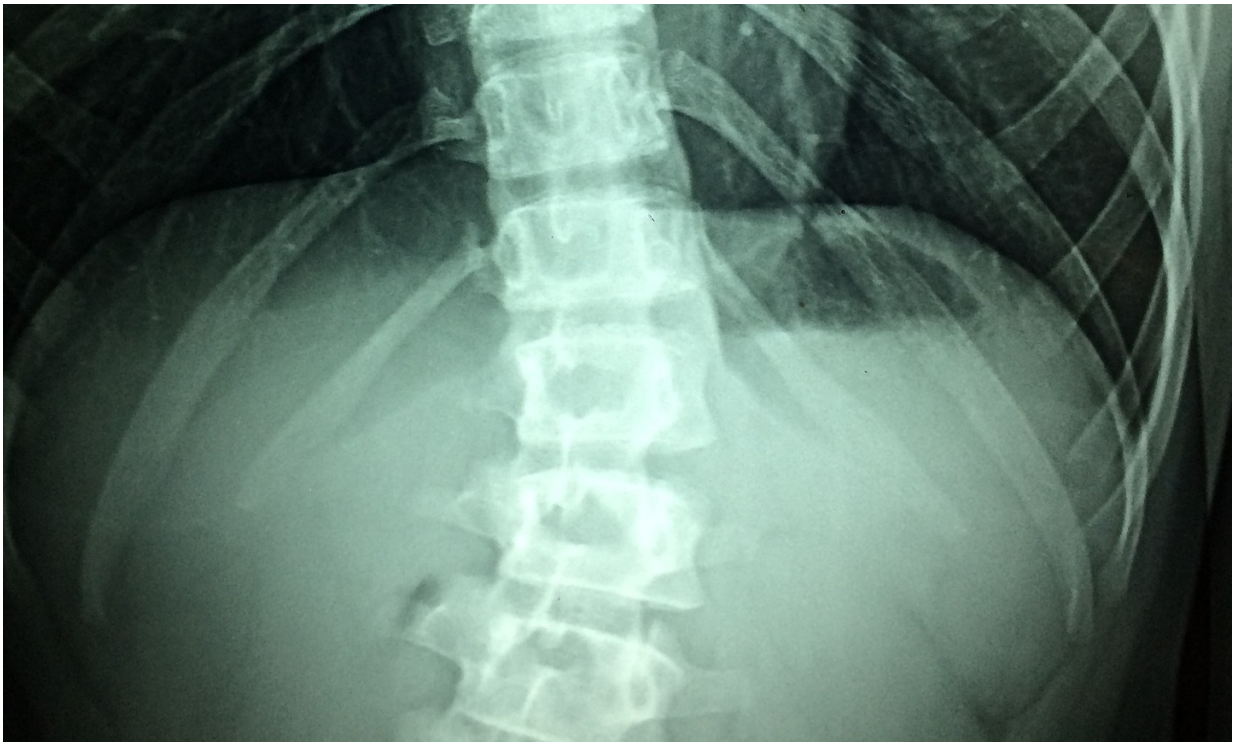

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Meningiomas, tumors of the membranes (meninges) surrounding the brain and spinal cord, are the most common tumors of the central nervous system. Although most meningiomas are low grade and cause few or no symptoms, a subset, called high-grade meningiomas, can cause serious neurologic and cognitive problems and have high mortality rates.

Meningiomas are treated with surgery and in some cases radiation, but there are few other effective therapies, and even with optimal therapy, recurrences are common: About half of all patients with intermediate (grade 2) meningiomas will have a recurrence within 5 years of treatment, and 90% of patients with the most advanced (grade 3) meningiomas will experience recurrences within 5 years.

Only about half of all patients with recurrent aggressive grade 2 meningiomas and none with grade 3 disease can be expected to survive for 10 years.

But as Priscilla Brastianos, MD, from the Mass General Cancer Center and Harvard Medical School (HMS) and colleagues now report, a class of cancer drugs known as immune checkpoint inhibitors can slow disease progression and offer hope for longer survival of patients with high-grade meningiomas.

They report their findings in the open-access journal *Nature Communications*.

"In the past our understanding of the molecular underpinnings of meningiomas has been limited, and it has only been within the last few years that we have begun to understand the immune microenvironment of meningiomas," says Brastianos.

Recent studies have suggested that the tumor microenvironment—the environment around a tumor that includes blood vessels, immune cells and chemical signals—may suppress immune responses to meningiomas. Immune checkpoint inhibitors such as pembrolizumab block PD-1, a protein that prevents the immune system from mounting a defense against tumors. The drug effectively releases the brakes on the immune system, allowing it to accomplish its tumor-identifying and destroying functions.

To see whether immunotherapy could be effective in patients with high-grade meningiomas, Brastianos and colleagues conducted a phase 2 trial in which they treated 25 patients with recurrent and progressive grade 2 or 3 meningiomas with the immune checkpoint inhibitor pembrolizumab (Keytruda).

The trial met its primary goal, with nearly half of all patients alive and without evidence of disease progression for at least 6 months. Half of the patients were still alive 20 months after treatment.

Side effects of therapy were similar to those seen in other studies of pembrolizumab and were manageable.

"Our study shows that it's both practical to conduct clinical trials for meningiomas—a disease for which there have been very few studies—and that pembrolizumab has promising activity against meningiomas, and needs to be studied further in larger groups of patients," says Brastianos.

More information: Priscilla K. Brastianos et al, Phase 2 study of pembrolizumab in patients with recurrent and residual high-grade meningiomas, *Nature Communications* (2022). DOI: 10.1038/s41467-022-29052-7

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