

# Lethal extracranial hemorrhage due to intracranial clivalchordoma: An autopsy case

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## ABSTRACT

We present a case of a 48-year-old man's unexpected death affected by a relapsed clivalchordoma. After partial excision surgery of the neoplasm, he manifested 5 days later, in conditions of well-being, a sudden lethal extracranial hemorrhage from nose and mouth. The autopsy examination and the subsequent histological investigations did not allow us to clarify the exact origin of the bleeding. Based on the negativity of the accurate examinations performed, the extent of the bleeding, and the findings highlighted by the means of the nuclear magnetic resonance (NMR) carried out a few days before death, we have considered reasonable to localize the source of hemorrhage in the intrapetrous tract of the left internal carotid artery. Since this is a unique event, never previously documented, we believe that our report may be of interest to the scientific community.

**KEY WORDS:** Clivalchordoma, extracranial hemorrhage, forensic pathology, sudden death

## INTRODUCTION

Chordoma is a rare primary malignant bone tumor arising from the primitive notochord.<sup>[1]</sup> It can occur at any point of the axial skeleton and when intracranial it has predominantly an extradural localization.<sup>[2]</sup> It may occur at any age, showing slow progression symptoms closely related to its localization.<sup>[3]</sup> It causes intense lytic activity on the surrounding bone structures and is characterized by high invasiveness and marked tendency to relapse and metastasize.<sup>[1]</sup> The diagnosis is often made too late and for this reason, the prognosis is usually poor and death usually occurs due to compression and/or infiltration of the brain stem<sup>[4]</sup> or due to the tumor-related intracranial hemorrhages.<sup>[2,5,6]</sup> However, cases of nonlethal intracranial hemorrhagic events<sup>[7,8]</sup> are also described. In literature, finally, only one case of nonlethal extracranial nose-bleeding is reported, as the first manifestation of a clivalchordoma.<sup>[1]</sup> We present the first case of lethal extracranial hemorrhage related to a clivalchordoma and, given the uniqueness of this event, we consider it of interest to the scientific community, both clinical and forensic.

## CASE HISTORY

A 48-year-old man affected by a clivalchordoma underwent trans labyrinthine surgery. The subsequent histological and immunohistochemical examinations performed on the surgical piece confirmed the diagnosis of chordoma (CK and brachyury positive; c-kit positive; PDGFR-beta negative; focal cytoplasmic and membrane beta-catenin

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positive; Ki67 proliferative index 5%). He was then subjected to postoperative radiotherapy treatment. Two years later, a new nuclear magnetic resonance detected an expansive relapsed lesion in the clival area, infiltrating the tissues up to the petrous apex and the intrapetrous tract of the left internal carotid artery. He underwent transsphenoidal surgery to

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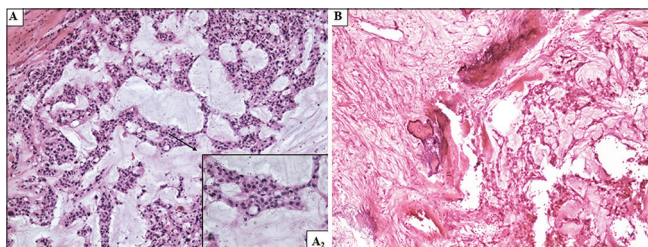
remove at least in part the neoplasm, with a regular postoperative period. Suddenly on the 5<sup>th</sup> day he manifested a massive hemorrhage from the upper airways (nose and mouth), causing immediate death. 3 days after an autopsy was performed at the Institute of Forensic Medicine of Milan.

### Autopsy findings

Macroscopically, dried blood staining of the nasal and buccal orifices was observed. At autopsy, a large amount of blood (2L) was found in the oral cavity, airways, and digestive tract. At the skull examination, there was the absence of both extradural and intradural hemorrhage. The surgical site, located between the clivus and the petrous part of the left temporal bone, was filled by insertions of adipose tissue. Macroscopically there were no lesions of the sphenoid sinus and of the cavernous tract of the left internal carotid artery. The brain appeared slightly edematous and free of pathological lesions, both compressive and hemorrhagic. Likewise, all the other internal organs were free of injuries. During the autopsy, samples of viscera, the entire petrous bone, and surrounding soft tissues were collected and fixed in 10% buffered formalin.

### Histologic examination

All the viscera samples and the entire petrous bone - after decalcification in 14% HCl solution (Histodecal®) - underwent standard histological processing. In addition to the H and E staining, periodic acid/Schiff, Alcian blue pH 2.5, Weigert's resorcin-fuchsin and Goldner's Masson trichrome techniques were performed. At microscopic observation, several neoplastic foci were documented almost on the entire petrous bone and the surrounding soft tissues, morphologically consistent with the diagnosis of chordoma [Figure 1A, A<sub>2</sub> and B]. The myxoid cellular stroma appeared strongly positive to the Alcian blue pH 2.5 staining [Figure 2A]; there were also some PAS-positive intracytoplasmic foci [Figure 2B]. In the middle portion of the sample, neoplastic foci showed recent intratumoral hemorrhage, with extension to surrounding tissues [Figure 2C and D]. Weigert's resorcin-fuchsin staining did not highlight structural alterations of the walls of the intracranial arterial vessels [Figure 2E], as a potential origin of the bleeding. Goldner's Masson trichrome staining also confirmed the same findings [Figure 2F and F<sub>2</sub>].



**Figure 1:** In A (H and E, 100 x), multiple cellular foci of relapsed neoplasm with cito-histological features consistent with cordoma, incorporated in the myxoid stroma. In A<sub>2</sub> (H and E, 400 x), detail of vacuolated cells. In B (H and E, 100 x), remains of bone trabeculae infiltrated by the tumor and surrounded by abundant fibrous tissue

## DISCUSSION

We presented a case of unexpected death due to extracranial hemorrhagic shock (nose and mouth) that occurred in a man suffering from relapsed clival chordoma. This occurrence, to the best of our knowledge, represents a unique case worthy of mention, since acute lethal hemorrhagic events reported in the literature so far have had all an exclusively intracranial localization.<sup>[2,5-6]</sup> The only known event of extracranial chordoma-related hemorrhage involved a case of nonlethal nose-bleeding that occurred as the first manifestation of a clival chordoma.<sup>[1]</sup> All the above-mentioned cases of hemorrhagic events have been found to have in common the failure in identifying the exact source of the bleeding.

In our case, the autopsy examination, although carefully performed, failed to clarify the origin of the lethal extracranial hemorrhage. Therefore, lacking the presence of both significant compressive effects on brain structures and intracranial bleeding, we identified the cause of death as acute hemorrhagic shock. Likewise, even the histological examination focused on the entire petrous bone, including the intrapetrous tract of the left carotid artery, didn't show the origin of the hemorrhage. In the view of the above-mentioned findings, we considered reasonable to attribute the bleeding to the impairment of a major arterial vessel, potentially identifiable as the intrapetrous tract of the left carotid artery. This hypothesis is also corroborated by the findings that emerged from the nuclear magnetic resonance performed antemortem. In our specific case, the research was overall further burdened by some not negligible concurrent factors, such as the far from the easy exploration of the anatomical tract involved, the intense destructive lytic activity of chordoma, the multiple surgical procedures and the effects of radiotherapy treatments performed.

We presented a unique case of lethal extracranial hemorrhagic manifestation arising from a clival chordoma. Although rare, this event represents a concrete occurrence in patients with chordoma of the clivus, reason why we believe it is important to make clinicians and forensic pathologist aware of the possible onset of a sudden and massive lethal extracranial hemorrhage.

### Ethical approval

This article does not contain any studies with living human participants performed by any of the Authors. All the studies conducted followed the guidelines provided by Legislation and the National Bioethical Committee.

### Informed consent

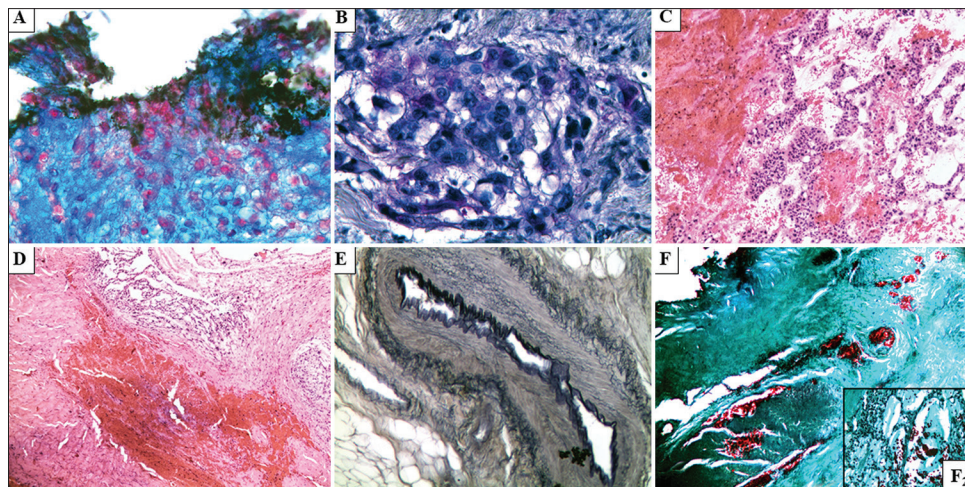
The author(s) declared that the Investigating Magistrate authorized all the forensic investigations performed in this study, in accordance to the Italian Law.

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Nil.

### Conflicts of interest

There are no conflicts of interest.



**Figure 2:** In A (alcian blue pH 2.5, 100 x), positivity of the myxoid stroma with the extension of the neoplasm up to the upper bone margins. In B (periodic acid/Schiff, 400 x), focal positivity. In C (H and E, 50 x), hemorrhagic infiltration of peritumoral tissues; in D (H and E, 100 x), widespread intratumoral hemorrhagic foci. In E (Weigert's resorcin-fuchsin, 50 x), the section of intracranial arterial vessel with undamaged walls. In F (Goldner's Masson trichrome, 50 x), arterial vessel free of injuries; in F<sub>2</sub> (Goldner's Masson trichrome, 200 x), intratumoral hemorrhagic foci

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