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Is the frontal sinus immune to carcinoma? A retrospective study and review of the literature

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Abstract

Background Frontal sinus carcinoma is commonly seen as an extension of the ethmoid sinus, overlying skin, or lacrimal gland. The existence of this disease has been unclear. We aimed to describe the occurrence of primary frontal sinus carcinoma.

Methods We conducted a systematic literature review and a retrospective review of the medical records at our institution in the past 10 years.

Results Sixty-four articles were included in the literature review. Most frontal sinus carcinomas involved surrounding structures as the sphenoid or ethmoid sinus, and a primary origin in the frontal sinus could not be confirmed. No cases of primary frontal sinus carcinoma were identified at our hospital.

Conclusion Isolated primary frontal sinus carcinoma, if exists, is very rare. There is uncertainty regarding the primary origin of frontal sinus carcinoma in most studies. The frontal sinus seems to be immune from primary carcinoma. Further studies are needed to explain such immunity.

Key points

- Frontal sinus being the primary site for carcinoma is extremely rare.
- The diagnosis of primary frontal sinus carcinoma remains questionable, as it is commonly seen as an extension of the ethmoid sinus, overlying skin, or lacrimal gland.
- There was uncertainty regarding the primary origin of the frontal sinus tumor in most studies.
- No cases of primary frontal sinus carcinoma were identified at our hospital.
- The cause of the rarity of occurrence of primary frontal sinus carcinoma is still not known.
- Further studies are needed to explain such invulnerability or immunity.

Keywords Frontal sinus, Paranasal sinus neoplasms

Background

Primary or isolated carcinoma of the frontal sinus is extremely rare, reported to account for 0.3–1.0% of all paranasal sinus carcinomas and only 0.009–0.03% of all head and neck cancers [1–5]. Over a 40-year course of practice in the field of head and neck surgery at Kasr Al Aini Hospital, we have not encountered a case of

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primary carcinoma of the frontal sinus. Many clinicians, even those with a special interest in the disease, may not encounter any case of primary carcinoma of the frontal sinus during their professional careers. Frontal sinus carcinoma is commonly seen as extension of the ethmoid sinus, overlying skin, or lacrimal gland [2, 3]. Many authors have even questioned the existence of this disease. Moreover, the cause of such invulnerability or immunity is unclear. A systematic review of the corresponding literature and a retrospective search of the reported cases may offer the gateway to this puzzle. Therefore, this study aimed to describe the occurrence of primary frontal sinus carcinoma. To achieve this, we performed a systematic review of the literature to evaluate whether the frontal sinus could be susceptible to carcinoma. In addition, we performed a retrospective study of the medical records on primary carcinoma of the frontal sinus at our institute.

Methods

This study was reviewed and approved by the institutional review board of Kasr Al Aini Hospital, Cairo Medical School, Egypt (approval number: N-14-2023). Informed consent to participate was obtained. The data were de-identified.

Systematic review

The study included published articles available in PubMed and Google Scholar databases from their inception until 6th of November 2022. The Preferred Reporting Items for Systematics Reviews and Meta-Analyses (PRISMA) guidelines were followed. The search was performed by two different researchers. *The inclusion criteria were as follows:* (1) all patients with primary squamous cell carcinoma of the frontal sinus and (2) case reports, randomized controlled trials, and observational studies. *The exclusion criteria were as follows:* (1) extension of the tumor to the frontal sinus from an adjacent primary site, (2) metastatic carcinoma of the frontal sinus from distant malignancy, and (3) pathology other than carcinomas like lymphoma, sarcoma, inverted papilloma, and nonneoplastic conditions.

PubMed was searched using terms as follows: ((frontal AND (sinus)) AND (carcinoma) with applying automatic filters, species filter including only human studies, and language filter including only articles in English. Google Scholar was searched using terms as follows: “frontal sinus carcinoma” OR “frontal sinus tumors” OR “frontal sinus tumor” OR “frontal sinus malignancy” OR “frontal sinus malignancies,” anywhere in the article — articles in English only — excluding citations. This was followed by manual exclusion of all duplicated and irrelevant articles.

Evaluation of risk of bias was done using Joanna Briggs Institute checklists.

Retrospective study

The medical records on paranasal sinus carcinoma from the Department of Pathology at our institute over the past 10 years (January 2013 to December 2022) and from the Department of Otolaryngology over the past 5 years (January 2018 to December 2022) were reviewed. All paranasal sinus carcinoma cases were evaluated to identify frontal sinus carcinoma. Only cases of primary or isolated sinus carcinoma were targeted.

Results

Systematic review

The selection process for studies included within the systematic review was done according to PRISMA guidelines (Fig. 1).

We could not estimate the total number of reported cases in the literature because many cases were reported in multiple case reports, case series, and retrospective studies. In total, 541 records were found in both databases. After the removal of 153 duplicates, 388 articles were included. Furthermore, only cases of primary frontal sinus carcinoma were included, so, more 311 articles citing benign or metastatic tumors and pathologies other than carcinoma, and irrelevant studies, were excluded. Moreover, the remaining full-text 77 articles were assessed for eligibility, and 22 articles were excluded. Finally, only 55 articles were included [1–55].

Retrospective study

The retrospective study of medical records did not reveal any case of primary carcinoma of the frontal sinus.

Discussion

Sinonasal carcinomas constitute 3–5% of all head and neck cancers [1–5]. Patients are generally asymptomatic in the early stages; hence, approximately two-thirds of patients present with stage IV tumors. The near location to important structures like the skull base and orbit presents a therapeutic challenge. Several authors have questioned the existence of primary carcinoma of the frontal sinus [3, 56] and even tried to provide an explanation for this inconceivable observation [54, 57]. Several studies including large number of patients showed no carcinoma primarily involving the frontal sinus, supporting the inconceivable observation [20, 27, 34, 58–62].

Large retrospective studies of paranasal sinus malignancies generally revealed the rarity of primary frontal sinus carcinoma in addition to uncertainty regarding the primary origin of the tumor [10]. Most of these tumors were included in extensive lesions involving the

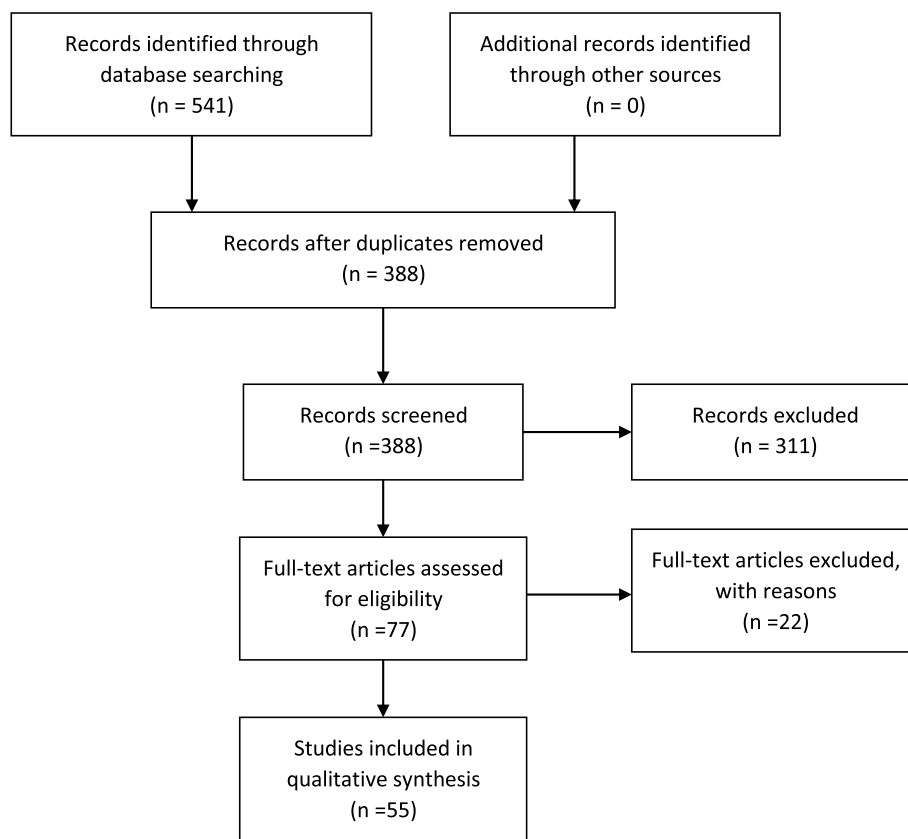


Fig. 1 PRISMA flow chart

adjacent ethmoid sinus [2–5, 13–22, 25–32, 35, 38, 41, 42, 48, 49, 54]

Various reports have described extensive carcinoma-tous lesions, with the skin, ethmoid sinus, or the lacri-mal gland being the origin of frontal sinus carcinoma. There is no solid evidence regarding the exact origin of the primary frontal sinus carcinoma [6, 13, 21, 27, 51].

One of the largest series included 13,295 patients with sinonasal malignancies enrolled between 1973 and 2011. The frontal sinus was involved in 1–2% cases. No information was provided to establish whether these represented primary isolated frontal sinus lesions or extension of adjacent structures [63].

Another considerably large series on frontal sinus malignancies was conducted. A 30-year search of the SEER database revealed 171 cases, including approximately 116 cases with different types of carcinomas [1]. Most patients presented with extensively advanced local disease with or without regional or distant metas-tasis. Hence, it was not possible to identify the primary origin of these tumors. It also revealed that overall prognosis for patients with frontal sinus malignancies is poor, with a 5-year overall survival rate of 31 to 50%.

Prognosis was most commonly related to extent of dis-ease and local recurrence [1].

Other series on paranasal sinus malignancies studied for 10–19 years reported two to three cases of primary frontal sinus carcinoma [34, 39, 43, 46]. There was inad-equate characterization regarding the origin of these rare tumors; in particular, nearly all described extensive tumors invaded more than one subsite.

In many reports, because primary tumors of fron-tal and sphenoid sinuses are rare, they were grouped and analyzed with the advanced primary tumors of the ethmoid sinus [2, 9, 25, 34, 35, 51, 61, 64].

Moreover, old reports also increase uncertainty regard-ing the true origin of possible or suspected primary frontal sinus carcinoma. The first report of frontal sinus carcinoma was published in 1907 [65], as cited in 2014 [21]. A systematic review of the French literature in 1948 [66] cited 5 years later [57] identified 31 cases of primary carcinoma of the frontal sinus. The Indian literature 50 years ago reported two consecutive cases of primary carcinoma of the frontal sinus and cited an earlier report of 102 cases [48, 67]. Such large case series reported 50 and 75 years ago, in the absence of modern radiology

and the advance in pathology, should raise doubt about regarding whether the cases were of primary carcinoma of the frontal sinus or an extension from surrounding lesions or even metastatic.

Malignancy has been associated with cholesteatoma of the frontal sinus [45, 68]; the occurrence of these two rare conditions in the same patient was questioned [52]. Primary frontal sinus carcinoma was claimed to be associated with frontal mucopyoceles [3, 41, 47]. The origin of these tumors was debated and suspected to be the lacrimal gland [1, 29]. A case report of primary frontal sinus carcinoma related to osteomyelitis was published [40]. Metastasis could not be ruled out owing to the rapid nature and aggressive nature of the lesion. Primary frontal sinus carcinoma was identified on top of a frontal sinus inverted papilloma [7, 24] in conjunction with ethmoid [24] and sphenoid [7] lesions, which does not substantiate the frontal sinus being the origin of the carcinoma. One case report described two separate synchronous carcinomas in the right frontal sinus in the same patient, i.e., squamous cell carcinoma and adenoid cystic carcinoma. It should be noted that this patient had sinus irrigation with thorotrast 30 years before, which is a carcinogenic material [44].

Limitations of our study include being single-center study, although our center is a major tertiary referral center. Our retrospective study also included relatively limited number of years (5 years at the otolaryngology department and 10 years at the pathology department). In our systematic review, we noticed a high risk of bias in most of studies reporting primary frontal sinus carcinoma because it was not possible to confirm the site of origin of most of the reported cases of primary frontal sinus carcinoma in the literature, as they either characterized extensive tumors or did not provide accurate imaging studies to prove the exact site of origin of the tumor especially in early studies.

Conclusions

Primary frontal sinus carcinoma is rare, constituting < 5% of sinonasal carcinomas in most reports. More than a century since the earliest reports of primary frontal sinus carcinoma [65], various published articles followed. Most of the reported cases of frontal sinus carcinoma were extensive tumors involving multiple structures such as the orbit and lacrimal gland, ethmoid sinus, and skin of the forehead. There was uncertainty regarding the primary origin of the frontal sinus tumor in most studies. In some reports, cases were grouped with advanced primary tumors of the ethmoid or sphenoid sinuses. Large series collecting cases over many years did not reveal any case of primary frontal sinus carcinoma at our institution. In fact, several authors

have questioned the existence of primary frontal sinus carcinoma [56] and even provided an explanation for this inconceivable observation [57]. The present systematic review and retrospective study endorses the infrequency or absenteeism of primary frontal sinus carcinoma.

The mucosal immune system in the intestines, urogenital tract, and respiratory system plays a protective against toxins and microbial diseases [69]. The role of the immune system against cancer is not entirely understood. Nevertheless, the mucosal immune system may play a role in protecting the frontal sinus to a great extent and may solve this puzzle. The frontal sinus seems to be immune from primary carcinoma. However, further studies are needed to explain such invulnerability or immunity.

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Authors' contributions

MZ contributed in data collection for the retrospective study and revision of the article. AME contributed in methodology, search of PubMed and Google Scholar databases, and scientific writing of the article. MR had the idea of the work, contributed in search of PubMed and Google Scholar databases which were searched by him and AME each of them individually, and revision of the whole article. All authors read and approved the final manuscript.

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Availability of data and materials

Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

Declarations

Ethics approval and consent to participate

This study was reviewed and approved by the institutional review board of Kasr Al Aini Hospital, Cairo Medical School, Egypt (approval number: N-14-2023). Informed consent to participate was obtained. The data were de-identified.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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