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BRIEF REPORT

Not Only Meningitis but Also Epiglottitis: An Emerging Clinical Presentation of Invasive Meningococcal Disease

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The rebound of invasive meningococcal disease cases in France since the fall of 2022 was accompanied by an increase in adult epiglottitis. These cases were provoked mainly by isolates of serogroup W belonging to the clonal complex 11 of *Neisseria meningitidis*. Awareness and surveillance should be reinforced.

Keywords. epiglottitis; invasive meningococcal disease; serogroup W.

Neisseria meningitidis is a usual host of the human nasopharynx, where it may be carried asymptomatically in the general population (isolates of asymptomatic carriage). However, meningococcal isolates can also cross the epithelial barrier of the nasopharynx to invade the blood and provoke invasive meningococcal disease (IMD). These invasive isolates usually belong to the so-called hyperinvasive genotypes belonging to a limited number of genetic lineages (also named clonal complexes) according to sequencing-based typing (multilocus sequence typing) [1]. The clinical presentations of IMD are diverse. They are dominated by the typical forms of bacteremia and meningitis; however, a wide range of other atypical presentations have also been described and have been recently reviewed by several authors. They are linked to the hematogenous spread of meningococci and their extrameningeal localization [2]. The proportions of these atypical forms vary according to age and isolates and can be underestimated. They represent significant proportions of IMD that may reach 15% for bacteremic pneumonia [3], but others remain rare, such as epiglottitis, necrotizing fasciitis, and other soft tissue infections [4].

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Moreover, the frequency of these atypical forms can vary with epidemiological changes such as those observed during the coronavirus disease 2019 (COVID-19) pandemic and after easing the COVID-19 restriction measures [5]. Indeed, we have recently observed an increasing number of meningococcal epiglottitis cases referred to our laboratory (the National Reference Centre for Meningococci and *Haemophilus influenzae* at the Institut Pasteur, Paris, France [NRCMHi]). The NRCMHi is a part of the French national surveillance of IMD, which is composed of the mandatory reporting of cases that are centralized by Santé Publique France according to the French case definition, as well as sending the isolates and samples with their metadata to the NRCMHi for full typing. The surveillance system of IMD in France showed good exhaustiveness (91%) as evaluated in 2005 [6].

Since the easing of COVID-19 restriction measures in France in October 2022, the NRCMHi received an unusual number of cases of IMD with epiglottitis that accompanied the rapid rebound of IMD cases observed in France [7]. Epiglottitis is characterized by swollen glottic tissues (edematous epiglottis) associated with fever, sore throat, dysphagia, and inaudible voice. The diagnosis can be confirmed by fiberoptic laryngoscopy and cervical computed tomography scan, which usually shows the edematous epiglottis obstructing the air pathway [8]. The bacteriological etiology is usually based on the detection of specific bacteria in the blood, although blood cultures in most cases remain negative [8]. Historically, epiglottitis was essentially due to infection with *H. influenzae* of serotype b (Hib). The introduction of conjugated Hib vaccine resulted in an important reduction in the number of cases and a subsequent change in microbiological etiologies that include *Streptococcus pneumoniae*, *Staphylococcus aureus*, *H. parainfluenzae*, and *Pseudomonas aeruginosa* [9, 10]. However, *N. meningitidis* is reported much less often for this clinical form. We aimed to analyze this signal by comparing IMD cases with epiglottitis before and after the COVID-19 pandemic.

METHODS

Isolates and samples for the 2015–June 2023 period were extracted from the NRCMHi database with data on age groups, serogroups, and clinical presentations (that were classified as associated or not with epiglottitis). Data were curated for duplicate entries. A total of 3024 cases were received during this period.

Antibiotic susceptibility testing of meningococci for penicillin G and cefotaxime with MIC gradient strips (E-test, bioMérieux, Marcy l'Etoile, France) was conducted, in accordance with the recommendations of the European

Table 1. Description and Bacteriological Characteristics of the Cases of Epiglottitis

Studied Period	Total No. of Cases	No. of Epiglottitis Cases (%)	Cases	Age, y	Year	Sex	Site	Group	Clonal Complex	MIC Penicillin G[a]	MIC Cefotaxim[b]
2015 to March 15, 2020	2211	5 (0.2)	1	42.14	2017	M	Blood	W	11	0.032(S)	0.003 (S)
			2	87.74	2017	F	Blood	W	11	0.032 (S)	0.002 (S)
			3	82.25	2018	F	Blood	C	11	0.047 (S)	0.004 (S)
			4	80.12	2019	F	Blood	Y	23	0.064 (S)	0.004 (S)
			5	72.54	2019	F	Blood	C	11	0.064 (S)	0.006 (S)
March 16, 2020–September 2022	345	0 (0)									
October 2022–June 2023	465	8 (1.7)	6	52.94	Oct. 2022	F	Blood	W	22	0.19 (I)	0.006 (S)
			7	79.68	Dec. 2022	F	Blood	W	11	0.047 (S)	0.003 (S)
			8	82.88	2023	M	Blood	W	11	0.094 (S)	0.006 (S)
			9	86.48	2023	F	Blood	Y	23	0.19 (I)	0.008 (S)
			10	66.87	2023	F	Blood	W	11	0.125 (I)	0.012 (S)
			11	84.39	2023	F	Blood	W	11	0.094 (S)	0.012 (S)
			12	74.35	2023	M	Blood	Y	23	0.19 (I)	0.012 (S)
			13	69.77	2023	F	Blood	W	11	0.047 (S)	0.004 (S)

Abbreviations: I, intermediate; MIC, minimal inhibitory concentration; S, susceptible.

[a]MIC for penicillin G < 0.125 mg/L for S and ≥ for I.

[b]MIC for cefotaxim ≤0.125 mg/L for S.

Committee on Antimicrobial Susceptibility Testing (EUCAST; https://www.eucast.org/).

The cases were categorized into 3 periods: 2015 to March 15, 2020, which corresponded to the first lockdown period in France (prepandemic period), March 16, 2020, to September 2022 (pandemic period), and October 2022 to June 2023 (postpandemic period). Typing of the isolates was performed using whole-genome sequencing as previously reported [7].

RESULTS

Our screening among the total number of 3024 cases of IMD revealed the presence of 13 cases of IMD with epiglottitis (0.5%) that were distributed among the 3 periods, respectively, as follows: 2211 cases of IMD with 5 cases of epiglottitis (0.2%), 345 cases of IMD with no cases of epiglottitis, and 468 cases of IMD with 8 cases of epiglottitis (1.7%).

Table 1 depicts the characteristics of the meningococcal epiglottitis cases and the corresponding isolates. All cases were among adults >40 years of age, ranging between 42 years and 86 years with a median of 79 years, but a majority were females (10/13), corresponding to a male:female ratio of 0.3, which is lower than the male:female ratio of IMD (0.96) that was observed in France during the period 2015–2022 [7]. Previous studies have also suggested an increase in the incidence of epiglottitis in adults [2, 11]. All 13 cases were associated with sepsis. Our data also suggest that serogroup W is overrepresented among epiglottitis cases (8 of the 13 cases, 62%). Moreover, the proportion in serogroup W was even higher for the period postpandemic (75%) than the period prepandemic (40%). However, the low number of cases prevents reliable statistical analysis. These proportions were higher than the overall proportion for serogroup W among all IMD cases for the whole period from 2015 to June 2023 (16%). They also remained higher than the proportions for serogroup W during the prepandemic, pandemic, and postpandemic periods of 14%, 14%, and 26%, respectively. Serogroup Y was also overrepresented, with 3 cases of IMD with epiglottitis (23%). This observation suggests that epiglottitis is linked to serogroups W and Y, as also suggested by previous studies [2, 12].

DISCUSSION

The emergence of a new lineage of the cc11 since 2010 in Europe was associated with an increase in atypical clinical presentations such as abdominal presentations but also epiglottitis. During the 3 epidemiologic years (2010–2011 to 2012–2013) in England and Wales, the number of epiglottitis cases was 5 (4%) among 129 IMDW cases [4]. This proportion was similar to that observed in our study for the postpandemic period, with 6 (5%) cases among the 120 IMDW cases during the 9 months that accounted for the postpandemic period in our study (Table 1). These data further suggest a rapid rebound of IMDW after easing the COVID-19 restriction measures, with the fear of an increase in the atypical clinical presentations that may delay management. The reasons for this increase remain to be explored. The study of the role of changes of pharyngeal microbiota during the pandemic period may be informative.

The meningococcal isolates were susceptible to beta-lactams with only 4 isolates of the 13 that showed reduced susceptibility (intermediate) to penicillin G (Table 1), and all were susceptible to third-generation cephalosporins (cefotaxim and ceftriaxone). This may guide the choice of antibiotic for empiric treatment pending the etiological diagnosis of septic epiglottitis. However, as all our cases are associated with

sepsis, treatment should also be according to the guidelines of IMD management.

However, vaccine-based prevention may be the most appropriate response for this situation. The implementation of ACWY vaccination needs to be urgently considered not only for children and adolescents but also for older adults, where the burden of the disease is increasingly notified [2]. ACWY vaccination is currently not recommended in the general population in France. Only vaccination against meningococci B and C is recommended in children <2 years of age [7]. The implementation of ACWY vaccination should provide direct protection in the targeted population but also indirect protection in nonvaccinated subjects through the reduction of acquisition and circulation of these isolates in the population.

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Potential conflicts of interest. All authors: no reported conflicts.

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